University of Alberta

The Impact of Pruritus on the Health-Related Quality of Life of Patients with Chronic Plaque Psoriasis

by

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Abstract

Few studies have assessed the effect of pruritus severity, a subjective symptom that is difficult to measure, on health-related quality of life (HRQL). One-hundred-thirty-six psoriasis patients completed a modified pruritus questionnaire (if applicable), RAND-36, Dermatology Life Quality Index (DLQI), and Hospital Anxiety and Depression Scale (HADS). A questionnaire to quantify pruritus severity, Itch Severity Scale (ISS), was developed based on the modified pruritus questionnaire using exploratory factor analysis, studies of internal consistency, inter-item correlation analyses, and correlation analyses with HRQL scores. Evidence for ISS validity and reliability was acquired. Using ISS scores, it was determined that pruritus severity was significantly associated with poorer HRQL (RAND-36, DLQI) but not with anxiety or depressive symptomatology (HADS). This research yields a new self-report questionnaire for use in clinical evaluation and research and provides evidence that pruritus, which may be overlooked in medical practice, is a potentially debilitating symptom warranting medical attention and treatment.

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List of Abbreviations

DLQI	Dermatology Life Quality Index
HADS	Hospital Anxiety and Depression Scale
HRQL	Health-related quality of life
ISS	Itch Severity Scale
MHC	Mental Health Composite
PHC	Physical Health Composite
RAND-36	RAND-36 Health Status Inventory
SAPASI	Self-Administered Psoriasis Area and Severity Index
SD	Standard deviation
SF-36	Short Form-36
VAS	Visual analogue scale

Chapter 1

Introduction

The notion of quality of life encompasses perceptions related to almost all aspects of daily existence. In the medical community, the definition has been narrowed to health-related quality of life (HRQL), which may be defined as "optimum levels of mental physical, role (e.g., work, parent, carer, etc.) and social functioning, including relationships, and perceptions of health, fitness, life satisfaction and well-being" (Bowling, 1995). In the past, HRQL has not been an influential issue, or even of much consideration, within the medical community – likely the reflection of a system that traditionally focuses on the physical sequelae of disease while disregarding the accompanying psychosocial facets. However, the recent shift toward patient-oriented care has prompted the application of HRQL in various areas of health care, including the evaluation of health-care interventions, policy-making (e.g. resource allocation), and the measurement of the impact of chronic disease. With respect to the latter, measuring HRQL is critical because physiologic measures do not always correlate with functional capacity and well-being (Guyatt *et al*, 1993). Also, it is commonplace to encounter differing responses between patients satisfying the same clinical criteria (Guyatt *et al*, 1993). HRQL assessment may also be used to evaluate the impact of symptoms of disease. However, in order to do so accurately, particularly for subjective sensory symptoms such as pain or pruritus, it is important to have methods by which to accurately gauge symptom severity.

HRQL studies have recently been applied to the field of dermatology. Generally, the medical community does not perceive the field of dermatology to be of equal importance to specialties addressing internal organs, because diseases of the skin do not have the same overall impact on lifespan (Baker, 1993; Russell, 1994). However, the underlying purpose of health services is to improve HRQL – hence, the impact of a disease should not be based solely on the detriment to the number of life years but also on the detriment to the quality of those years. Health is defined by the World Health Organization as a "state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity" (World Health Organization, 1947; World Health Organization, 1948). This suggests that in order to truly appreciate the importance of a disease or condition in health, one must evaluate it from the perspective of these various aspects, all of which are encompassed in the concept of HRQL.

The quantification of HRQL detriment provides a value that allows comparison between various disease populations, and thus a means to assess the relative importance of the various medical fields with respect to HRQL impact. An appreciation of the impact of skin diseases on HRQL is thus paramount regarding appropriate and fair health policy-making and resource allocation, and most relevant to the education of health professionals with reference to the importance of not only quantity but also quality of life.

1.1 Literature Review

Psoriasis, a chronic skin condition affecting 1-3% of the general population, has been the focus of much HRQL research. Well-circumscribed, circular erythematous papules or plaques with a grey, dry scale are the clinical hallmarks of the disease. Reports suggest that 67-80% of patients with psoriasis experience pruritus as a symptom (Gupta *et al*, 1988; Krueger *et al*, 2001; Szepietowski *et al*, 2004).

Wahl *et al* (2002) interviewed twenty-two people with psoriasis to assess the effects of the disease on daily life. Data suggested that the disease became all-consuming and took control of patients' actions, thoughts, and feelings. These all-consuming feelings were wide ranging and included: depression, hopelessness, anxiety, and aggression. Patients also felt ashamed for being 'different and inadequate'. Psoriasis greatly affected social functioning as a result of its impact on self-image. Interviewees described experiences of rejection and staring because of the look of their skin. Some described desires to hide from people. In effect, the body "can no longer support the positive social function, which in turn may lead to social isolation" (Wahl *et al*, 2002). This social vulnerability was deemed a core consequence of living with psoriasis. When asked to describe being symptom-free, many interviewees said it was a state of emotional freedom and the liberty to experience 'living life' (Wahl *et al*, 2002).

The above qualitative assessment highlights the important facets of life on which psoriasis imparts a negative effect. Rapp *et al* (1999) attempted to quantify these effects. The SF-36 questionnaire was used to compare the HRQL impact of psoriasis to that of

other diseases. The results demonstrate that psoriasis imparts a negative impact on both physical and mental components of HRQL. Interestingly, the impact was, overall, more negative than other diseases that are considered of greater burden than skin diseases, such as hypertension, type 2 diabetes, and depression. This comparison suggests that even though psoriasis does not threaten life itself, it can severely threaten HRQL.

Other studies have also compared psoriasis to other diseases. Nearly half of a surveyed population in the United States indicated they would sooner have a medical condition typically thought of as more dangerous, like asthma or hypertension, than a skin condition like psoriasis (Weiss *et al*, 2002). Moreover, 46, 42, and 32% of a surveyed psoriasis population considered it would be 'better' or 'the same' to have diabetes, asthma, or bronchitis, respectively (Finlay and Coles, 1995). Of the patients who also had the comparative diseases of diabetes, asthma and bronchitis, 87, 80, and 77% respectively considered it would be 'better' or 'the same' to have the comparative disease (Finlay and Coles, 1995).

Jowett and Ryan (1985) interviewed 100 people with acne, psoriasis, or eczema to determine the impact of these conditions. Interestingly, when asked about the worst aspects of their condition, itch became a common theme. Forty percent of those with acne reported itchy skin and 87% of those with psoriasis considered itch an important feature of the disease. Insofar as those with eczema were concerned, all considered itching a significant symptom. As one interviewee with eczema explained: "It's like when you have an itch and scratch it but that doesn't relieve it. It's raw with eczema, you can't feel

the soreness just the itching, the blood runs and you still scratch" (Jowett and Ryan, 1985). This vivid illustration stresses the potentially tormenting and debilitating nature of pruritus.

Pruritus can be detrimental to daily life, a notion commonly underestimated and unaddressed in clinical practice. It has been shown to be associated with significant psychiatric morbidity (Gupta *et al*, 1988; Picardi *et al*, 2000; Sampogna, Picardi *et al*, 2003) and in some cases with suicidal ideation (Gilchrest, 1984). Gupta *et al* (1988) demonstrated a direct relationship between pruritus severity and severity of depression. Further, therapy-based improvement of pruritus was associated with improvement in depressive symptoms. However, whether pruritus is a causative factor in depression is unclear because a depressed clinical state may lessen pruritus threshold (Gupta *et al*, 1994). Another study pertaining to pruritus in 108 psoriasis patients showed 35% became more agitated, 24% became depressed, 30% had difficulty concentrating, and 9% became more anxious because of pruritus (Yosipovitch *et al*, 2000).

The effect of pruritus on mood has been assessed in other disease populations. The symptom was reported to cause agitation in 36-55% (Yosipovitch *et al*, 2001; Yosipovitch, Ansari *et al*, 2002; Yosipovitch, Goon *et al*, 2002), depression in 8-37% (Yosipovitch *et al*, 2001; Yosipovitch, Ansari *et al*, 2002; Yosipovitch, Goon *et al*, 2002), and difficulty concentrating in 43% (Yosipovitch, Ansari *et al*, 2002) and 63% (Yosipovitch, Goon *et al*, 2002) of the sample populations.

Sleep disturbances are another consequence of chronic pruritus, perhaps contributing to the mental health burden. Pruritus associated with atopic dermatitis has been shown to cause frequent waking and a reduced sleeping efficiency (Stores *et al*, 1998), which can lead to difficulty awakening, daytime tiredness, and irritability. Further, in children with atopic dermatitis, difficulty falling asleep and frequent waking have been shown to correlate with daytime behavior and discipline problems (Dahl *et al*, 1995). A study of pruritus in patients with psoriasis reported difficulty falling asleep due to pruritus in 69% and awakening due to pruritus in 66% of patients (Yosipovitch *et al*, 2000). Similar studies in patients with chronic idiopathic urticaria (Yosipovitch, Ansari *et al*, 2002), atopic dermatitis (Yosipovitch, Goon *et al*, 2002), and end-stage renal disease (Yosipovitch *et al*, 2001) demonstrated that 62%, 84%, and 61% had difficulties falling asleep due to pruritus, respectively. In these same populations, 64%, 79%, and 44% were awakened by pruritus, respectively.

Few studies have examined the overall HRQL detriment associated with pruritus. The symptom has been shown to be significantly associated with poorer HRQL in patients with cholestatic liver disease (Younossi *et al*, 2000), chronic venous insufficiency (Duque *et al*, 2005), and post renal transplant (Moloney *et al*, 2005). Lastly, Sampogna *et al* (2003) examined the impact of 25 dermatological conditions and found that pruritus was 1 of 4 conditions deemed to have the greatest impact on HRQL.

The need for studies addressing mental and physical HRQL in patients with pruritus provides the impetus for a study to quantify and clinically interpret the association between pruritus severity and HRQL, anxiety, and depressive symptomatology.

The quantification of the degree and characteristics of pruritus is difficult because of its subjective nature. For research purposes, itching can be recorded and assessed by intraneuronal recordings of C-fibre electrical activity using microneurography (Hagermark and Wahlgren, 1992), by recording scratch movements through various techniques (Hagermark and Wahlgren, 1992; Yosipovitch *et al*, 2003) and via subjective methods that include the use of self-report scales (Hagermark and Wahlgren, 1992). However, these approaches may not be suitable to measure the severity of pruritus because intensity is only one facet of this multidimensional symptom.

Generally, the intensity of pruritus, and not its other qualities, such as how the symptom is perceived by the patient or its effects on daily life, has been the focus of previous studies. This is partly due to a lack of standardized questionnaires to quantify pruritus severity. However, two relevant instruments have recently been developed. The first is based on the long form of the McGill Pain Questionnaire (Melzack, 1975) and includes a detailed list of sensory and affective descriptors, but it does not include any questions regarding effect on HRQL (Darsow *et al*, 2001). This self-report questionnaire takes about 30 minutes to complete, hence is quite time consuming and demanding. The second instrument (Yosipovitch *et al*, 2001) is based on the short form of the McGill Pain Questionnaire (Melzack, 1975) and probes sensory and affective dimensions, as well as

effects on HRQL. However, it is interviewer-administered, a significant practical limitation. Further, neither instrument has a method of scoring that quantifies pruritus severity specifically, nor patient burden generally. Thus, we contend that the development of a practical questionnaire assessing pruritus severity and resulting patient burden is required for both clinical evaluation and research.

1.2 Study Objectives

The first objective was to develop a self-report questionnaire to quantify pruritus severity and provide evidence of its validity and reliability. The purpose of this was to allow for the characterization of pruritus severity for the subsequent objectives.

The second objective was to measure and compare the HRQL of patients with chronic plaque psoriasis associated with varying degrees of pruritus. It was hypothesized that patients with chronic plaque psoriasis associated with moderate-severe pruritus would have worse HRQL than those with none-mild pruritus.

The final objective was to measure and compare levels of anxiety and depressive symptomatology in patients with chronic plaque psoriasis associated with varying degrees of pruritus. It was hypothesized that patients with chronic plaque psoriasis associated with moderate-severe pruritus would have greater anxiety and depressive symptomatology than those with none-mild pruritus.

References

Baker DR: Prioritization of health services: the Oregon Basic Health Services Act and its implications for dermatologists and patients with dermatologic disease. *Dermatol Clin* 11:241-249, 1993

Bowling A: *Measuring Disease*. Buckingham: Open University Press, 1995, p 3

Dahl RE, Bernhisel-Broadbent J, Scanlon-Holdford S, Sampsom HA, Lupo M: Sleep disturbances in children with atopic dermatitis. *Arch Pediatr Adolesc Med* 149:856-860, 1995

Darsow U, Scharein E, Simon D, Walter G, Bromm B, Ring J: New aspects of itch pathophysiology: Component analysis of atopic itch using the 'Eppendorf Itch Questionnaire'. *Int Arch Allergy Immunol* 124:326-331, 2001

Duque MI, Yosipovitch G, Chan YH, Smith R, Levy P: Itch, pain, and burning sensation are common symptoms in mild to moderate chronic venous insufficiency with an impact on quality of life. *J Am Acad Dermatol* 53:504-508, 2005

Finlay AY, Coles EC: The effect of severe psoriasis on the quality of life of 369 patients. *Br J Dermatol* 132:236-244, 1995

Gilchrest BA: Cutaneous sensation and pathophysiology of pruritus. In: *Pathophysiology of Dermatologic Diseases*. Soter NA, Baden HP (eds). New York: McGraw-Hill, 1984, p 73-80

Gupta MA, Gupta AK, Kirkby S, *et al*: Pruritus in psoriasis: A prospective study of some psychiatric and dermatologic correlates. *Arch Dermatol* 124:1052-1057, 1988

Gupta MA, Gupta AK, Schork NJ, Ellis CN: Depression modulates pruritus perception: A study of pruritus in psoriasis, atopic dermatitis, and chronic idiopathic urticaria. *Psychosom Med* 56:36-40, 1994

Guyatt GH, Feeny DH, Patrick DL: Measuring health-related quality of life. *Ann Intern Med* 118:622-629, 1993

Hagermark O, Wahlgren CF: Some methods for evaluating clinical itch and their application for studying pathophysiological mechanisms. *J Dermatol Sci* 4:55-62, 1992

Jowett S, Ryan T: Skin disease and handicap: An analysis of the impact of skin conditions. *Soc Sci Med* 20:425-429, 1985

Krueger G, Koo J, Lebwohl M, Menter A, Stern RS, Rolstad T: The impact of psoriasis on quality of life: Results of a 1998 National Psoriasis Foundation patient-membership survey. *Arch Dermatol* 137:280-284, 2001

Melzack R. The McGill Pain Questionnaire: Major properties and scoring methods. *Pain* 1:277-299, 1975

Moloney FJ, Keane S, O'Kelly P, Conlon PJ, Murphy GM: The impact of skin disease following renal transplantation on quality of life. *Br J Dermatol* 153:574-578, 2005

Picardi A, Abeni D, Melchi CF, Puddu P, Pasquini P: Psychiatric morbidity in dermatological outpatients: An issue to be recognized. *Br J Dermatol* 143:983-991, 2000

Ramsay B, O'Reagan M: A survey of the social and psychological effects of psoriasis. *Br J Dermatol* 118:195-201, 1988

Rapp SR, Feldman SR, Exum ML, Fleischer AB, Reboussin DM: Psoriasis causes as much disability as other major medical diseases. *J Am Acad Dermatol* 41:401-407, 1999

Russell PS: Dermatology in the Oregon Plan with implications for health care plans in other states. *Arch Dermatol* 130:709-712, 1994

Sampogna F, Picardi A, Melchi CF, Pasquini P, Abeni D: The impact of skin disease on patients: Comparing dermatologists' opinions with research data collected on their patients. *Br J Dermatol* 148:989-995, 2003

Stores G, Burrows A, Crawford C: Physiological sleep disturbance in children with atopic dermatitis: A case control study. *Pediatr Dermatol* 15:264-268, 1998

Szepietowski JC, Reich A, Wisnicka B: Pruritus and psoriasis. *Br J Dermatol* 151:1284, 2004

Wahl AK, Gjengedal E, Hanestad BR: The bodily suffering of living with severe psoriasis: In-depth interviews with 22 hospitalized patients with psoriasis. *Qual Health Res* 12:250-261, 2002

Weiss SC, Kimball AB, Liewehr DJ, Blauvelt A, Turner ML, Emanuel EJ: Quantifying the harmful effect of psoriasis on health-related quality of life. *J Am Acad Dermatol* 47:512-518, 2002

World Health Organization: *Constitution of the World Health Organization.* Geneva: WHO, 1947

World Health Organization: *Official Records of the World Health Organization*, No. 2, p.100. Geneva: WHO, 1948

Yosipovitch G, Ansari N, Goon, A, Chan YH, Goh CL: Clinical characteristics of pruritus in chronic idiopathic urticaria. *Br J Dermatol* 147:32-36, 2002

Yosipovitch G, Goon A, Wee J, Chan YH, Goh CL: The prevalence and clinical characteristics of pruritus among patients with extensive psoriasis. *Br J Dermatol* 143:969-973, 2000

Yosipovitch G, Goon ATJ, Wee J, Chan YH, Zucker I, Goh CL: Itch characteristics in Chinese patients with atopic dermatitis using a new questionnaire for the assessment of pruritus. *Int J Dermatol* 41:212-216, 2002

Yosipovitch G, Greaves MW, Schmelz M: Itch. *Lancet* 361:690-694, 2003

Yosipovitch G, Zucker I, Boner G, Gafter U, Shapira Y, David M: A questionnaire for the assessment of pruritus: Validation in uremic patients. *Acta Derm Venereol* 81:108-111, 2001

Younossi ZM, Kiwi ML, Boparai N, Price LL, Guyatt G: Cholestatic liver diseases and health-related quality of life. *Am J Gastroenterol* 95:497-502, 2000

Chapter 2

Development and Validation of an Instrument for the Measurement of Pruritus Severity

2.1 Introduction

Pruritus is perhaps the most commonly described symptom in dermatology. It is associated with numerous skin conditions such as atopic dermatitis, urticaria, and psoriasis, as well as with a variety of systemic conditions, including chronic renal failure and hepatic cholestasis. It is a potentially debilitating symptom associated with considerable psychiatric morbidity (Gupta *et al*, 1988; Picardi *et al*, 2000; Sampogna, Picardi *et al*, 2003), sleep disturbances (Dahl *et al*, 1995; Stores *et al*, 1998; Yosipovitch *et al*, 2000), and an overall reduced health-related quality of life (HRQL) (Duque *et al*, 2005; Moloney *et al*, 2005; Sampogna, Picardi *et al*, 2003; Younossi *et al*, 2000).

Quantification of the degree and characteristics of pruritus is difficult because of its subjective nature. For research purposes, itching can be recorded and assessed by intraneuronal recordings of C-fibre electrical activity using microneurography (Hagermark and Wahlgren, 1992), by recording scratch movements through various techniques (Hagermark and Wahlgren, 1992; Yosipovitch *et al*, 2003), and via subjective methods that include the use of self-report scales (Hagermark and Wahlgren, 1992). However, these approaches may not be suitable to measure the severity of pruritus because itch intensity is only one facet of this multidimensional symptom.

Generally, the intensity of pruritus, and not its other qualities, such as how the symptom is perceived by the patient or its effects on daily life, has been the focus of previous studies. This is due in part to a lack of standardized questionnaires to quantify pruritus severity. However, two relevant instruments have recently been developed. The first is based on the long form of the McGill Pain Questionnaire (Melzack, 1975) and includes a detailed list of sensory and affective descriptors, but it does not include any questions regarding effect on HRQL (Darsow *et al*, 2001). It is a self-report questionnaire that takes about 30 minutes to complete, hence is quite time consuming and demanding. The second instrument (Yosipovitch *et al*, 2001) is based on the short form of the McGill Pain Questionnaire (Melzack, 1975) and probes sensory and affective dimensions, as well as effects on HRQL. However, it is interviewer-administered, a significant practical limitation. Further, neither instrument quantifies pruritus severity specifically, nor patient burden generally.

Thus, we contend that the development of a practical questionnaire assessing pruritus severity and resulting patient burden is required for both clinical evaluation and research. An ideal instrument would capture patients' perception of pruritus severity and allow the comparison of severity among different disease populations as well as the assessment of the effectiveness of therapy. The purpose of this study was to develop a self-report questionnaire to quantify pruritus severity based on the instrument constructed by Yosipovitch *et al*, and to assess its validity and reliability.

2.2 Methods

2.2.1 Overview

The instrument previously developed by Yosipovitch *et al* was modified to a self-report format. The modified self-report version of Yosipovitch *et al*'s instrument (hereafter referred to as the "modified pruritus questionnaire") was administered to patients with chronic plaque psoriasis along with the RAND-36 Health Status Inventory and Dermatology Life Quality Index. Exploratory factor analysis, studies of internal consistency, inter-item correlation analyses, and correlation analyses with HRQL scores were used to determine which components of the modified pruritus questionnaire were most appropriate to include in the final instrument, the Itch Severity Scale (ISS). The final ISS was then assessed for construct validity, internal consistency reliability, and test-retest reliability. This study was approved by the Health Research Ethics Board at the University of Alberta.

2.2.2 Sample

Subjects were consecutively recruited from phototherapy and dermatology clinics in Alberta. Inclusion criteria were as follows: (1) stable chronic plaque psoriasis involving a minimum 5% body surface area; (2) the psoriasis had been present for a minimum of 6 months; (3) chronic psoriasis-associated pruritus, defined as at least 2 episodes of itch per week, the itch occurring several times a day, lasting for more than 5 minutes, being bothersome, and had been present for a minimum of 6 weeks; and subjects were (4) between the ages of 18 and 70, (5) able to give informed consent, and (6) able to complete the questionnaires in English.

2.2.3 Measures

The questionnaire package (Appendix A) included questions on demographics and comorbidities, plus the following 4 measures:

Self-Administered Psoriasis Area and Severity Index (SAPASI). The SAPASI (Fleischer *et al*, 1994) is a self-report instrument with good evidence to support its validity and reliability in measuring psoriasis severity (Feldman *et al*, 1996; Fleischer *et al*, 1994; Sampogna, Sera *et al*, 2003). A visual analogue scale (VAS) for psoriasis global assessment was also included, from which missing SAPASI scores were imputed using a linear regression formula, derived from subjects with complete data on both measures.

Modified pruritus questionnaire. As above, an interviewer-administered instrument was previously developed by Yosipovitch *et al* (2001) (Appendix B). It was developed for the characterization and evaluation of pruritus. It has no method of scoring with which to quantify severity of the symptom. The instrument was modified for this study to a self-report format and included questions on the following: duration; frequency; pattern; body surface area involved; intensity as measured by 5-point Likert scale and VAS; current antipruritic treatment and efficacy; accompanying symptoms; description of itch sensation and affective descriptors; effect of daily activities on pruritus; and effect of pruritus on sleep, mood, ability to concentrate, diet, sexual desire, and sexual function.

RAND-36 Health Status Inventory. The RAND-36 (Hays, 1998) is a widely used 36-item generic measure of health status comprised of the same questions as the well-known

Short Form-36, but that uses different scoring methodology. Evidence suggests that the RAND-36 scores may be more accurate (Simon *et al*, 1998; Taft *et al*, 2001; Johnson and Maddigan, 2004), prompting its use, over the Short Form-36, in this study. It measures eight dimensions of health status and has two summary scores: the Physical Health Composite (PHC) and Mental Health Composite (MHC). A score from 0 to 100 is calculated for each of the eight subscales, with higher scores indicating better HRQL. The PHC and MHC are calculated as norm-based T-scores. There is considerable data to support the instrument's validity and reliability (Hays, 1998). As suggested by the developer, mean imputation is performed for missing RAND-36 data (Hays, 1998).

Dermatology Life Quality Index (DLQI). The DLQI (Finlay and Khan, 1994) is a skin-specific HRQL questionnaire with evidence for validity and reliability (Lewis and Finlay, 2004). Scores range from 0 (no impairment of life quality) to 30 (maximum impairment). A question left unanswered is scored 0 and if two or more questions are left unanswered the questionnaire is not scored (Finlay and Khan, Accessed 12/12/2005).

2.2.4 Procedure

Patients were briefly interviewed to determine if they met the aforementioned inclusion criteria. Those satisfying inclusion criteria were invited to take home a questionnaire package to be completed at their convenience. A reminder letter was sent if the questionnaire package had not been returned within two weeks.

2.2.5 Itch Severity Scale Development

Multiple strategies were used to select the relevant items from the modified pruritus questionnaire to comprise the final ISS. Components that had a relatively weak correlation with pruritus severity, based on preliminary factor analysis and expert opinion, were eliminated. The remaining, candidate items, were then subjected to exploratory factor analysis (Fayers and Hand, 1997). Principal component analysis with varimax rotation was applied to the candidate items to provide information regarding the nature of the contribution by each item to the measurement of pruritus severity.

Candidate items for the final scale were further evaluated based on internal consistency reliability and inter-item correlation analyses. Correlation analyses with HRQL scores were also performed based upon the hypothesis that more severe pruritus is associated with poorer HRQL. Thus, graded correlations in the appropriate direction were interpreted as indicating a greater association with pruritus severity. In addition, the aspects measured by each candidate item were compared to eliminate potentially redundant questions. Lastly, for each question, ambiguous or missing responses were noted to predict interpretative or other problems relating to the respective questions. Candidate items were subsequently chosen for the ISS based on the statistical analyses, while attempting to maintain a clinically logical combination that addressed all facets deemed important. Statistical analyses were conducted using SPSS 13.0; p-values < 0.05 were interpreted as statistically significant.

2.2.6 Instrument Validity

Construct validity of the ISS was evaluated through correlations with the accompanying three HRQL measures. Based on the premise that pruritus severity affects HRQL, it was hypothesized *a priori* that ISS scores would correlate with the HRQL scores, i.e. higher pruritus severity would be associated with lower HRQL. It was also hypothesized at the outset that the ISS scores would correlate more strongly with the DLQI scores than with the PHC and MHC scores of the RAND-36, because a skin-specific measure should be more sensitive to differences in HRQL caused by a skin condition than a generic measure of health status. Correlations were measured with Pearson's correlation coefficient (r) and interpreted as follows: $r \leq 0.3$ was interpreted as a weak correlation, $0.3 < r < 0.5$ as a moderate correlation, and $r \geq 0.5$ as a strong correlation (Guyatt *et al*, 1993).

2.2.7 Instrument Reliability

We assessed both internal consistency and test-retest reliability (Hays *et al*, 1993). Internal consistency reliability was determined using the Cronbach's alpha coefficient. To estimate the test-retest reliability of the ISS, the modified pruritus questionnaire was mailed to a random sample of the participants to complete again two weeks following initial questionnaire completion. Pearson's correlation coefficient (r) and intra-class correlation coefficients were used to estimate the test-retest reliability of the ISS based on responses to the modified pruritus questionnaire. We considered the minimum acceptable values for Cronbach's alpha, Pearson's correlation coefficient (r), and intra-class correlation coefficients to be 0.7 for group-level comparison and 0.9 for individual comparison (Hays *et al*, 1993).

2.2.8 Clinical Interpretation of ISS Scores

We defined a clinically important difference for the ISS based on comparisons with suggested clinically important differences in scores for the PHC and MHC of the RAND-36 (3-5 points) (Hays and Morales, 2001), and DLQI (2-5 points) (Hongbo *et al*, 2005) using the respective linear regression formulae.

2.3 Results

A total of 93 subjects completed the initial questionnaire package (Table 2.1). Most subjects were Caucasian (93.5%), married (64.5%), and employed (71.0%) (Table 2.1). The modified pruritus questionnaire was mailed to 40 of the subjects in the test-retest subsample. Thirteen subjects responded in the retest, between 11 and 17 days following initial completion, with a median of 15 days between responses. There were no statistically significant differences in demographic characteristics between the initial and retest samples (Table 2.1).

2.3.1 Candidate Item Assessments

Eleven candidate items were identified from the modified pruritus questionnaire: item 1 (days and hours per week of itch), item 2 (itch description A), item 3 (itch description B), item 4 (frequency), item 5 (pattern), item 6 (effect on sleep), item 7 (effect on mood), item 8 (effect on sexual desire/function), item 9 (itch intensity using Likert scale), item 10 (itch intensity using VAS), and item 11 (body surface area involved).

Exploratory factor analysis. The principal component analysis identified two meaningful factors. The first factor, which could be termed pruritus severity, explained 50.8% of the total variance. The loadings onto the first factor of items 1 and 11 were negligible and items 4 and 5 were moderate (Table 2.2). All other items had high loadings (i.e., >0.5) onto this overall factor, indicating significant contribution to the measurement of the severity construct (Table 2.2). The second factor, which includes the more temporal aspects, explained 12.3% of the total variance. Items 1, 4, 5, and 11 all had high loadings onto this factor (Table 2.2).

Inter-item correlation analyses. Of the 55 inter-item correlations, 11 were weak, 28 were moderate, and 16 were strong (Table 2.3). In general, items 1, 8, and 11 had relatively weaker inter-item correlations. The strongest correlations were between items 2 and 3 as well as between items 9 and 10, as expected since these pairs measure similar aspects. Items 2 and 3 are both descriptors, while items 9 and 10 both measure itch intensity but in different response formats (i.e., Likert versus VAS).

Correlations with HRQL scores. Overall, item correlations were stronger with the DLQI than with the PHC and MHC scores (Table 2.4), as predicted. Correlations showed inverse relationships, such that higher itch item score was associated with lower HRQL. Correlations ranged from -0.169 to -0.488 with the PHC, -0.102 to -0.414 with the MHC, and 0.219 to 0.546 with the DLQI.

All items except 1 and 5 had statistically significant correlations with the PHC. In terms of magnitude, items 6 and 7 had moderate correlations with the PHC and the remainder had weak correlations (Table 2.4).

All items except 1, 4, and 5 had statistically significant correlations with the MHC. Correlations were moderate between the MHC and items 2, 3, 6, 7, 8, 9, and 10. The remainder had weak correlations (Table 2.4).

Item 6 had a strong correlation with the DLQI and item 1 had a weak correlation. The other items had moderate correlations with the instrument. All were statistically significant (Table 2.4).

Internal consistency reliability. Cronbach's alpha coefficients were calculated for various candidate item combinations. Coefficient values were very similar, ranging from 0.793 to 0.827. All were above the minimum acceptable value. These data had negligible influence on item selection due to the lack of considerable differences in internal consistency reliability with varying item combinations.

Missing data. With respect to the data from this sample, 6 of the 11 items had 1 or 2 missing responses. Items 1, 3, and 8 had 5 missing (5.4%); item 2 had 6 missing (6.5%); and item 5 had 10 missing responses (10.8%).

2.3.2 Itch Severity Scale Development

Item 1 was removed based on low factor loading, relatively weaker inter-item correlations, and weak correlations with HRQL scores. It was also removed to eliminate a potential redundancy, as this item was thought to measure an aspect similar to that measured by item 4. This is evident by the fact that item 1 was strongly correlated with item 4 ($r = 0.601$), more so than with any other individual item.

Items 2 and 3 were similar in content, strongly correlated, and both performed reasonably well in our psychometric tests. Item 3 was chosen over item 2 in the final questionnaire due to its higher factor loading and stronger correlations with all HRQL scores.

Item 5 was removed based on weak correlations with PHC and MHC scores as well as due to a concern that the question was not easily understood – as reflected in the high number of missing responses.

Lastly, item 9 was chosen over item 10; both items assessed itch intensity, but in different response formats (i.e., Likert versus VAS). Differences in factor loadings and correlations with other items and HRQL scores were deemed insufficient to warrant the inclusion of a different response format in the new instrument and risk potential respondent confusion.

2.3.3 The Itch Severity Scale

The final Itch Severity Scale (Appendix C) consists of 7 of the original 11 candidate items: item 3 (itch description B), item 4 (frequency), item 6 (effect on sleep), item 7 (effect on mood), item 8 (effect on sexual desire/function), item 9 (itch intensity using Likert scale), and item 11 (body surface area involved).

Scoring of the ISS. The different component responses to each of the 7 questions are summed separately and divided by the highest possible total score for the respective question. The 7 values are then added together and multiplied by 3 to get a total out of 21. Total ISS scores can range from 0 (no pruritus) to 21 (most severe pruritus).

Twelve ISS scores were missing due to incomplete questionnaires. For the 81 calculable scores in this sample, the mean was 7.4 (SD 3.6) with scores ranging from 1.5 to 16.8 (Figure 2.1). There were no significant differences in demographic characteristics between subjects with ISS scores and those with missing scores.

Psychometric properties. The ISS scores correlated moderately with PHC scores ($r = -0.483$) and MHC scores ($r = -0.492$) and correlated strongly with DLQI scores ($r = 0.628$).

The ISS had an internal consistency reliability of 0.80, and strong test-retest reliability, with a Pearson's correlation coefficient (r) of 0.95 and an intra-class correlation coefficient of 0.95.

Interpretation of ISS scores. Relative to the PHC, an analogous clinically important difference in ISS scores is 2.1-3.5; based on the MHC it is 1.9-3.1; and compared to the DLQI it is 2.2-5.5. Overall, these indicate that a clinically important difference in ISS scores is approximately 2 points. Given the standard deviation of the mean ISS score observed in this sample (i.e., 3.6), this represents an effect size estimate of approximately 0.56, which is consistent with effect sizes calculated based on minimum clinically important differences of various instruments (Norman *et al*, 2003).

2.4 Discussion

Studies evaluating pruritus have tended to focus on the intensity of itch itself, often overlooking how the symptom is perceived by the patient. This is an important deficit in light of the subjective nature of itch. The assessment of severity as a reflection of subjective factors, in addition to itch intensity, may provide a more accurate representation of the pruritus, and hence prove to be potentially more useful in research and clinical practice. The goal of this study was to develop such an instrument to remedy the perceived deficit.

In this study, a questionnaire for the quantification of pruritus severity, the ISS, was developed based on an interviewer-administered pruritus assessment developed by Yosipovitch *et al* (2001). Results provide evidence of the new instrument's construct validity, as the ISS scores had moderate correlations with PHC and MHC scores of the RAND-36, and strong correlations with DLQI scores, confirming our hypothesis that itch is associated with reduced HRQL and that ISS shows a greater correlation with the skin-

specific instrument (DLQI). Internal consistency and test-retest reliability of the ISS were above the minimum acceptable value for group-level comparison. Furthermore, test-retest reliability was suggestive of sufficient reliability for individual comparisons.

While this provides initial evidence of the psychometric properties of the ISS, our results should be considered in light of several limitations. First, there is a lack of generalizability due to the limited inclusion criteria. The study was also limited by a small sample size. Further studies are required to add to the validity and reliability evidence of the ISS in other samples and clinics. Additional evidence of validity should include responsiveness of the ISS to change, as one desired function of the ISS is to assess treatment effectiveness. It is also important for further studies to determine the test-retest reliability of the ISS since this study only estimated test-retest reliability based on responses to the modified pruritus questionnaire. Lastly, a clinically important difference in ISS scores may be reassessed to confirm or refute the clinically important difference calculated in this sample. This would ideally be done as part of a study of responsiveness.

In summary, we developed the Itch Severity Scale, which, to our knowledge, is the first questionnaire for the quantification of global pruritus severity. Results of the study provide preliminary evidence of the instrument's validity and reliability. Its self-report nature and short time for completion make it practical, convenient and applicable for use in the clinic and through the mail. Such an instrument may be useful to compare pruritus

severity among different disease populations and to assess the effectiveness of treatments for pruritus.

Table 2.1: Demographic Characteristics

		Initial Sample (N = 93)	Retest Sample (N = 13)
Age	<30	12 (12.9%)	1 (7.7%)
	30-39	16 (17.2%)	2 (15.4%)
	40-49	21 (22.6%)	3 (23.1%)
	50-59	27 (29.0%)	5 (38.5%)
	60+	17 (18.3%)	2 (15.4%)
Sex	Male	45 (48.4%)	6 (46.2%)
	Female	48 (51.6%)	7 (53.8%)
Marital Status	Single	20 (21.5%)	2 (15.4%)
	Married/partnership	60 (64.5%)	10 (76.9%)
	Separated/divorced/ widowed	13 (14.0%)	1 (7.7%)
Education	Less than high school/ high school graduate	43 (46.2%)	4 (30.8%)
	College graduate	50 (53.8%)	9 (69.2%)
Main Activity	Working at job	66 (71.0%)	8 (61.5%)
	Looking for work	2 (2.2%)	1 (7.7%)
	Keeping house	5 (5.4%)	2 (15.4%)
	Student	0 (0.0%)	0 (0.0%)
	Unemployed due to disability	9 (9.7%)	1 (7.7%)
	Retired	11 (11.8%)	1 (7.7%)
Income	Under 10,000	9 (9.7%)	1 (7.7%)
	10,000-29,999	9 (9.7%)	0 (0.0%)
	30,000-49,999	16 (17.2%)	2 (15.4%)
	50,000-69,000	16 (17.2%)	2 (15.4%)
	70,000 and above	34 (36.6%)	8 (61.5%)
Ethnic	Caucasian	87 (93.5%)	13 (100.0%)
	Asian/Oriental	3 (3.2%)	0 (0.0%)
	East Indian	2 (2.2%)	0 (0.0%)
	Black	0 (0.0%)	0 (0.0%)
	Native Indian	1 (1.1%)	0 (0.0%)
Comorbidities		2.15 (SD 1.94)	1.46 (SD 1.27)
SAPASI Score		13.31 (SD 10.73)	9.51 (SD 6.26)

* $p < 0.05$

Table 2.2: Rotated Matrix Factor Loadings

	Factor 1 Loading	Factor 2 Loading
Item 1	0.039	0.841
Item 2	0.767	0.388
Item 3	0.806	0.351
Item 4	0.388	0.724
Item 5	0.419	0.587
Item 6	0.550	0.485
Item 7	0.754	0.081
Item 8	0.799	-0.050
Item 9	0.646	0.486
Item 10	0.622	0.446
Item 11	0.083	0.723

Table 2.3: Inter-Item Correlations

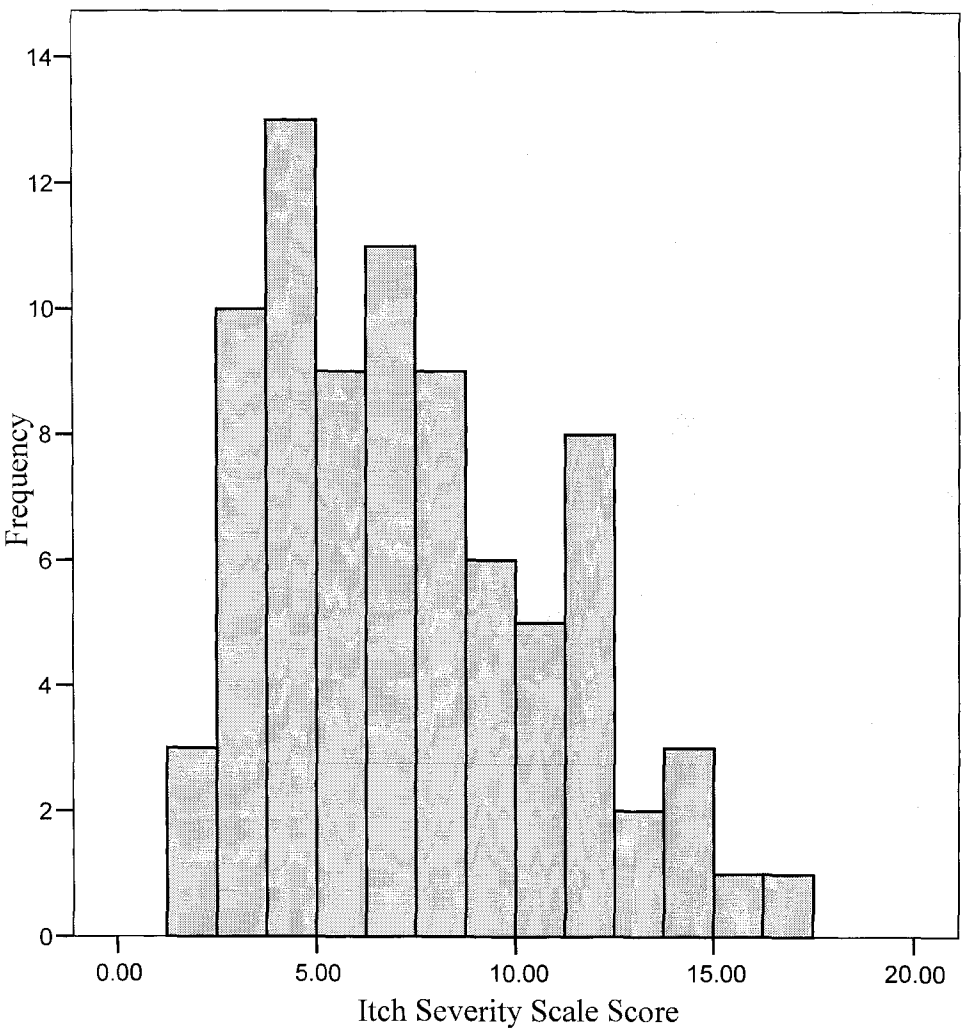
Item	1	2	3	4	5	6	7	8	9	10	11
1	1	0.335	0.265	0.601	0.392	0.361	0.169	0.177	0.412	0.366	0.458
2		1	0.953	0.585	0.469	0.499	0.501	0.384	0.575	0.539	0.289
3			1	0.561	0.505	0.486	0.516	0.412	0.622	0.558	0.244
4				1	0.616	0.381	0.345	0.303	0.490	0.442	0.393
5					1	0.456	0.359	0.187	0.489	0.395	0.387
6						1	0.417	0.322	0.558	0.589	0.356
7							1	0.524	0.403	0.357	0.239
8								1	0.286	0.336	0.151
9									1	0.832	0.246
10										1	0.215
11											1

Table 2.4: Candidate Item Correlations with Instrument Scores

	Physical Health Composite (T-Score)	Mental Health Composite (T-Score)	DLQI Score
Item 1	-0.169	-0.102	0.219*
Item 2	-0.243*	-0.332*	0.362*
Item 3	-0.251*	-0.352*	0.396*
Item 4	-0.296*	-0.194	0.307*
Item 5	-0.217	-0.112	0.377*
Item 6	-0.488*	-0.410*	0.546*
Item 7	-0.345*	-0.414*	0.367*
Item 8	-0.298*	-0.329*	0.480*
Item 9	-0.294*	-0.323*	0.389*
Item 10	-0.285*	-0.358*	0.450*
Item 11	-0.288*	-0.231*	0.383*

* $p < 0.05$

Figure 2.1: Itch Severity Scale Scores



References

Dahl RE, Bernhisel-Broadbent J, Scanlon-Holdford S, Sampsom HA, Lupo M: Sleep disturbances in children with atopic dermatitis. *Arch Pediatr Adolesc Med* 149:856-860, 1995

Darsow U, Scharein E, Simon D, Walter G, Bromm B, Ring J: New aspects of itch pathophysiology: Component analysis of atopic itch using the 'Eppendorf Itch Questionnaire'. *Int Arch Allergy Immunol* 124:326-331, 2001

Duque MI, Yosipovitch G, Chan YH, Smith R, Levy P: Itch, pain, and burning sensation are common symptoms in mild to moderate chronic venous insufficiency with an impact on quality of life. *J Am Acad Dermatol* 53:504-508, 2005

Fayers PM, Hand DJ. Factor analysis, causal indicators and quality of life. *Qual Life Res* 6:139-150, 1997

Feldman SR, Fleischer AB Jr, Reboussin DM, Rapp SR, Exum ML, Clark AR, Nurre L: The self-administered psoriasis area and severity index is valid and reliable. *J Invest Dermatol* 106:183-186, 1996

Finlay AY, Khan GK: Dermatology Life Quality Index (DLQI) – A simple practical measure for routine clinical use. *Clin Exp Dermatol* 19:210-216, 1994

Finlay AY, Khan GK: Dermatology Life Quality Index: Information and conditions concerning use. URL: www.dermatology.org.uk/portal/quality/dlqiinstruc.html (Accessed 12/12/2005)

Fleischer AB Jr., Rapp SR, Reboussin DM, Vanarthos JC, Feldman SR: Patient measurement of psoriasis disease severity with a structured instrument. *J Invest Dermatol* 102:967-969, 1994

Gupta MA, Gupta AK, Kirkby S, *et al*: Pruritus in psoriasis: A prospective study of some psychiatric and dermatologic correlates. *Arch Dermatol* 124:1052-1057, 1988

Guyatt GH, Feeny DH, Patrick DL: Measuring health-related quality of life. *Ann Intern Med* 118:622-629, 1993

Hagermark O, Wahlgren CF: Some methods for evaluating clinical itch and their application for studying pathophysiological mechanisms. *J Dermatol Sci* 4:55-62, 1992

Hays RD. *RAND-36 Health Status Inventory.* San Antonio: The Psychological Corporation, 1998

Hays RD, Anderson R, Revicki D: Psychometric considerations in evaluating health-related quality of life measures. *Qual Life Res* 2:441-449, 1993

Hays RD, Morales LS: The RAND-36 measure of health-related quality of life. *Ann Med* 33:350-357, 2001

Hongbo Y, Thomas CL, Harrison MA, Salek MS, Finlay AY: Translating the science of quality of life into practice: What do Dermatology Life Quality Index scores mean? *J Invest Dermatol* 125:659-664, 2005

Johnson JA, Maddigan SL: Performance of the RAND-12 and SF-12 summary scores in type 2 diabetes. *Qual Life Res* 13:449-456, 2004

Lewis V, Finlay AY: 10 years experience of the Dermatology Life Quality Index (DLQI). *J Investig Dermatol Symp Proc* 9:169-180, 2004

Melzack R. The McGill Pain Questionnaire: Major properties and scoring methods. *Pain* 1:277-299, 1975

Moloney FJ, Keane S, O'Kelly P, Conlon PJ, Murphy GM: The impact of skin disease following renal transplantation on quality of life. *Br J Dermatol* 153:574-578, 2005

Norman GR, Sloan JA, Wyrwich KW: Interpretation of changes in health-related quality of life: The remarkable universality of half a standard deviation. *Med Care* 41:582-592, 2003

Picardi A, Abeni D, Melchi CF, Puddu P, Pasquini P: Psychiatric morbidity in dermatological outpatients: An issue to be recognized. *Br J Dermatol* 143:983-991, 2000

Sampogna F, Picardi A, Melchi CF, Pasquini P, Abeni D: The impact of skin disease on patients: Comparing dermatologists' opinions with research data collected on their patients. *Br J Dermatol* 148:989-995, 2003

Sampogna F, Sera F, Mazzotti E, Pasquini P, Picardi A, Abeni D, IMPROVE Study Group: Performance of the self-administered psoriasis area and severity index in evaluating clinical and sociodemographic subgroups of patients with psoriasis. *Arch Dermatol* 139:353-358, 2003

Simon GE, Revicki DA, Grothaus L, Vonkorff M: SF-36 summary scores: Are physical and mental health truly distinct? *Med Care* 36:567-572, 1998

Stores G, Burrows A, Crawford C: Physiological sleep disturbance in children with atopic dermatitis: A case control study. *Pediatr Dermatol* 15:264-268, 1998

Taft C, Karlsson J, Sullivan M: Do SF-36 summary component scores accurately summarize subscale scores? *Qual Life Res* 10:395-404, 2001

Yosipovitch G, Goon A, Wee J, Chan YH, Goh CL: The prevalence and clinical characteristics of pruritus among patients with extensive psoriasis. *Br J Dermatol* 143:969-973, 2000

Yosipovitch G, Greaves MW, Schmelz M: Itch. *Lancet* 361:690-694, 2003

Yosipovitch G, Zucker I, Boner G, Gafter U, Shapira Y, David M: A questionnaire for the assessment of pruritus: Validation in uremic patients. *Acta Derm Venereol* 81:108-111, 2001

Younossi ZM, Kiwi ML, Boparai N, Price LL, Guyatt G: Cholestatic liver diseases and health-related quality of life. *Am J Gastroenterol* 95:497-502, 2000

Chapter 3

The Impact of Pruritus on the Health-Related Quality of Life of Patients with Chronic Plaque Psoriasis

3.1 Introduction

Within the medical community, there has been a shift from measuring disease and success of treatment based on physiologic aspects to a more patient-oriented care focus whereby improving health-related quality of life (HRQL) becomes focal. Inherent in this is gauging the impact of a disease not solely based on detriment to number of life years but also on the detriment to the quality of those years. This shift is especially relevant for dermatology relative to other specialties because of the perception that skin diseases are less important due to a lesser impact on lifespan (Baker, 1993; Russell, 1994). However, an appreciation of the impact of skin diseases on HRQL is paramount regarding health policy-making and resource allocation, and relevant to the education of health professionals.

HRQL encompasses the physical, mental, and social well-being of a person. In practical terms, HRQL can be applied to the assessment of effectiveness of disease-specific interventions, policy-making (e.g. resource allocation), and measurement of the impact of chronic disease. Psoriasis, a chronic skin condition affecting 1-3% of the general population, has been the focus of much HRQL research. Well-circumscribed, circular, red papules or plaques with a grey, dry scale are the clinical hallmarks of the disease.

Reports suggest that 67-80% of patients with psoriasis experience pruritus as a symptom (Gupta *et al*, 1988; Krueger *et al*, 2001; Szepietowski *et al*, 2004).

Pruritus, likely the most common symptom in dermatology, is associated with numerous skin conditions including atopic dermatitis, urticaria, and psoriasis. Pruritus is also a symptom of systemic conditions, including chronic renal failure and hepatic cholestasis. It is a debilitating symptom associated with psychiatric morbidity (Gupta *et al*, 1988; Picardi *et al*, 2000; Sampogna, Picardi *et al*, 2003) and sleep disturbances (Dahl *et al*, 1995; Stores *et al*, 1998; Yosipovitch *et al*, 2000). However, there is minimal literature evaluating the overall effect of pruritus on HRQL. One study compared 25 dermatological conditions and showed that pruritus was one of four deemed to have the greatest effect on HRQL (Sampogna, Picardi *et al*, 2003). An appreciation of the need for expanded studies addressing mental well-being and measurement of HRQL in patients with pruritus provided the impetus for the present study, the purpose of which was to determine if pruritus is associated with poorer HRQL, and greater anxiety and depressive symptomatology.

3.2 Methods

3.2.1 Overview

Subjects with chronic plaque psoriasis completed a questionnaire package that included an instrument for the characterization and evaluation of pruritus, generic and skin-specific HRQL measures, and a measure of anxiety and depression. Subjects were grouped based on pruritus severity (none-mild and moderate-severe). Questionnaire

scores were then compared between the two groups. This study was approved by the Health Research Ethics Board at the University of Alberta.

3.2.2 Sample

Subjects with chronic plaque psoriasis were consecutively recruited from phototherapy and dermatology clinics in Alberta. Inclusion criteria were as follows: (1) stable chronic plaque psoriasis involving a minimum 5% of body surface area, (2) the psoriasis had been present for a minimum of 6 months, (3) chronic pruritus associated with the psoriasis had been present or absent for a minimum of 6 weeks (chronic pruritus was defined as at least 2 episodes of itch per week, the itch occurring several times a day, lasting for more than 5 minutes, and being bothersome), and subjects were (4) between the ages of 18 and 70 years, (5) able to give informed consent, and (6) able to complete the questionnaires in English.

3.2.3 Measures

The questionnaire package (Appendix A) included questions on demographics and co-morbidities, plus the following 5 measures:

Self-Administered Psoriasis Area and Severity Index (SAPASI). The SAPASI (Fleischer *et al*, 1994) is a self-report measure of psoriasis severity with good evidence of validity and reliability (Feldman *et al*, 1996; Fleischer *et al*, 1994; Sampogna, Sera *et al*, 2003). Scores can range from 0 (no psoriasis) to 72 (most severe psoriasis). A visual analogue scale for psoriasis global assessment was also included, from which missing

SAPASI scores were imputed using a linear regression formula, derived from subjects with complete data on both measures.

Modified self-report version of Yosipovitch *et al*'s instrument. An interviewer-administered instrument was previously developed by Yosipovitch *et al* (2001) (Appendix B). It was developed for the characterization and evaluation of pruritus. It has no method of scoring which quantifies severity of the symptom. Yosipovitch's instrument was modified for this study to a self-report format and included questions on the following: duration; frequency; pattern; body surface area involved; intensity as measured by 5-point Likert scale and visual analogue scale; current antipruritic treatment and efficacy; accompanying symptoms; description of itch sensation and affective descriptors; effect of daily activities on pruritus; and effect of pruritus on sleep, mood, ability to concentrate, diet, sexual desire, and sexual function.

Based on this instrument, a self-report questionnaire was developed to quantify pruritus severity, the Itch Severity Scale (ISS) (Appendix C). The ISS includes questions on frequency of pruritus, intensity as measured by 5-point Likert scale, body surface area involved, a description of pruritus sensation, affective descriptors, and questions on how pruritus affects sleep, mood, ability to concentrate, sexual desire, and sexual function. Scores can range from 0 (no pruritus) to 21 (most severe pruritus). Subjects with missing ISS scores were not included in the analysis.

Psychometric properties of the ISS were assessed in a sample with chronic plaque psoriasis. With respect to construct validity, ISS scores correlated moderately with a generic measure and correlated strongly with a skin-specific measure of health status. Further, both internal consistency reliability and test-retest reliability values were above the minimum acceptable value for group-level analysis.

RAND-36 Health Status Inventory. The RAND-36 (Hays, 1998) is a widely used 36-item generic measure of health status comprised of the same questions as the well-known Short Form-36 (SF-36), but uses different scoring methodology. Evidence suggests that the RAND-36 scores may be more accurate (Simon *et al*, 1998; Taft *et al*, 2001; Johnson and Maddigan, 2004), prompting its use over the SF-36 in this study. There is considerable evidence of the instrument's validity and reliability (Hays, 1998). The RAND-36 assesses health on eight dimensions: physical functioning, role limitations due to physical problems, pain, general health, energy/fatigue, social functioning, role limitations due to emotional problems, and emotional well-being. A score from 0 to 100 is calculated for each scale, with higher scores indicating better HRQL. The eight dimensions can be combined into two summary scores: the Physical Health Composite (PHC) and Mental Health Composite (MHC), which are calculated as norm-based T-scores. Literature suggests that a 3-5 point difference in scale scores may be interpreted as clinically important (Samsa *et al*, 1999; Stewart *et al*, 1989; Weinberger *et al*, 1994). Mean imputation is performed for missing RAND-36 data (Hays, 1998).

Dermatology Life Quality Index (DLQI). The DLQI (Finlay and Khan, 1994) is a skin-specific HRQL questionnaire with evidence of validity and reliability (Lewis and Finlay, 2004). Scores range from 0 (no impairment of life quality) to 30 (maximum impairment). It is suggested that a 2-5 point difference may be interpreted as "a small effect on patient's overall HRQL" (Hongbo *et al*, 2005). A question left unanswered is scored 0 and if two or more questions are left unanswered the questionnaire is not scored (Finlay and Khan, Accessed 12/12/2005).

Hospital Anxiety and Depression Scale (HADS). The HADS (Zigmond and Snaith, 1983) is a 14-item questionnaire with two subscales measuring symptoms of anxiety and depression. Scores range from 0 (no anxiety or depression) to 21 (maximum anxiety or depression) for each subscale. Interpretation of the scores is well established: patients with subscale scores of 11 or higher are thought to have a higher probability of suffering from a mood disorder (Zigmond and Snaith, 1983). For the purpose of this study, probabilities of either anxiety or depression were reported as dichotomous variables (i.e., high or low for each). There is considerable evidence of its validity and reliability in a variety of patient populations, including ambulatory populations (Bjelland *et al*, 2002; Herrmann, 1997). Mean imputation is performed for missing HADS items, as has been previously described (Biringer *et al*, 2005).

3.2.4 Procedure

Patients were briefly interviewed to determine if they met the aforementioned inclusion criteria. Those satisfying inclusion criteria were invited to take home a questionnaire

package to be completed at their convenience. A reminder letter was sent if the questionnaire package had not been returned within two weeks.

3.3 Statistical Analysis

Subjects were classified into two groups based on ISS scores using a median split. The none-mild pruritus group consisted of subjects with ISS scores below the median, including those reporting no pruritus. The moderate-severe pruritus group consisted of subjects with ISS scores above the median.

Simple linear regression analyses were initially carried out with the RAND-36 or DLQI score as the dependent variable and pruritus group as the independent variable. Multiple linear regression analyses were then conducted with the dependent variable being RAND-36 or DLQI score and the independent variables being pruritus group and potential confounders (age, sex, marital status, education, number of comorbidities, and SAPASI score).

Simple and multiple logistic regression analyses were carried out with each of high probability of anxiety or depression from the HADS as the dependent variables and pruritus group without and with the aforementioned potential confounders as the independent variable(s), respectively.

Statistical analyses were conducted using SPSS 13.0; p-values < 0.05 were interpreted as statistically significant. Clinically important differences were interpreted as described above for each instrument.

3.4 Results

3.4.1 Patient Characteristics

Of the 196 questionnaires distributed, 136 were returned, for a response rate of 69%. Ninety-three subjects had psoriasis-associated pruritus while 43 were not experiencing this symptom. Twelve from the pruritus group were excluded because pruritus severity could not be determined due to incomplete questionnaires.

The none-mild and moderate-severe pruritus groups had 84 and 40 subjects, respectively. Subjects were primarily Caucasian (91.1%), married (65.3%), and employed (72.6%) (Table 3.1). There was a statistically significant difference in numbers of male and female between the two groups ($p = 0.032$), as well as significant differences in mean number of co-morbidities ($p = 0.023$) and mean SAPASI score ($p = 0.035$). There were no other statistically significant differences in demographic characteristics between the two pruritus groups (Table 3.1).

3.4.2 Pruritus and HRQL Scores

All RAND-36 mean scale scores were significantly lower in the moderate-severe pruritus group compared to the none-mild pruritus group, except the physical functioning scale ($p = 0.053$) (Table 3.2). Consequently, the PHC (Figure 3.1) and MHC (Figure 3.2)

summary scores were also significantly different (Table 3.2). After adjusting for the aforementioned potential confounders, we observed significant differences in mean scores between the two groups for the role-physical ($p = 0.044$), pain ($p = 0.001$), energy/fatigue ($p = 0.019$), social functioning ($p = 0.014$), and emotional well-being ($p = 0.043$) scales as well as the PHC ($p = 0.025$) and MHC ($p = 0.012$) summary scores (Table 3.2).

The mean DLQI score was significantly higher in the moderate-severe pruritus group than in the none-mild pruritus group (Table 3.2 and Figure 3.3). After adjusting for potential confounders, the mean difference between the two groups remained significant ($p < 0.001$) (Table 3.2).

3.4.3 Pruritus and HADS Scores

Both HADS anxiety (Figure 3.4) and depression (Figure 3.5) scores were significantly higher in the moderate-severe pruritus group than in the none-mild pruritus group (Table 3.3). In the none-mild pruritus group, there were 7 cases with a high probability of anxiety (8.3%) and 2 of depression (2.4%). In the moderate-severe pruritus group there were 12 cases with a high probability of anxiety (30.0%) and 2 of depression (5.0%).

There was a significant difference in likelihood of having anxiety between the two pruritus severity groups before adjusting for potential confounders – anxiety was 4.71 times more likely among the moderate-severe pruritus group than the none-mild pruritus group (95% confidence interval: 1.687 – 13.174) ($p = 0.003$) (Table 3.3). After adjusting

for potential confounders, however, the difference was no longer significant ($p = 0.096$) (Table 3.3). There were no significant differences in likelihood of having depression between the two groups, either unadjusted ($p = 0.450$) or adjusted ($p = 0.243$) analyses (Table 3.3).

3.5 Discussion

Few studies have formally evaluated the relationship between pruritus and HRQL. In this study, we demonstrated that pruritus is associated with poorer HRQL as measured by the RAND-36 and DLQI in patients with chronic plaque psoriasis. We, however, found no association with anxiety or depressive symptomatology as measured by the HADS.

We assessed HRQL differences between chronic plaque psoriasis patients with none-mild and moderate-severe pruritus using a generic measure of health status, the RAND-36. After adjusting for potential confounders, our results show a clinically important difference in all scales of the RAND-36, with the exception of physical functioning, between the none-mild and moderate-severe pruritus groups. This difference was statistically significant in the role-physical, pain, energy/fatigue, social functioning, and emotional well-being scales. Further, differences between the two groups were statistically significant and clinically important for both the PHC and MHC, after adjusting for potential confounders.

These results were reaffirmed with the skin-specific measure of health status, the DLQI, which also indicated statistically significant and clinically important differences in HRQL

between the none-mild and moderate-severe pruritus groups, after adjusting for the same potential confounders.

The results are in agreement with reported assessments in patients with cholestatic liver disease (Younossi *et al*, 2000), chronic venous insufficiency (Duque *et al*, 2005), and post renal transplantation (Moloney *et al*, 2005): these studies demonstrated pruritus was significantly associated with poorer HRQL using the SF-36, a modified Skindex-16, and the DLQI, respectively.

The HADS was used in our study to determine the difference in prevalence of anxiety and depressive symptomatology between chronic plaque psoriasis patients with none-mild and moderate-severe pruritus. After adjusting for potential confounders, we saw no differences in HADS scores between the two groups. This is contrary to the results of other studies, where pruritus has been shown to be significantly associated with psychiatric morbidity (Gupta *et al*, 1988; Picardi *et al*, 2000; Sampogna, Picardi *et al*, 2003) and in some cases with suicidal ideation (Gilchrest, 1984). Gupta *et al* (1988) demonstrated a direct relationship between pruritus severity and severity of depression, and therapy-based improvement of pruritus was associated with improvement in depressive symptoms. However, whether pruritus is a causative factor in depression is unclear because a depressed clinical state may lessen pruritus threshold (Gupta *et al*, 1994). Another study pertaining to pruritus in 108 psoriasis patients showed 35% percent became more agitated, 24% became depressed, 30% had difficulty concentrating, and 9% became more anxious because of pruritus (Yosipovitch *et al*, 2000).

The lack of relationship with the HADS scores also contradicts our own results observed with the RAND-36, where there was a relationship between pruritus severity and both the emotional well-being scale and the MHC. Possible explanations for the lack of a significant association between pruritus severity and HADS scores include the following: (1) the sample size was not large enough to detect a difference with the HADS, (2) the measurements are strategically different as the HADS addresses only the psychic symptoms of neurosis to diagnose mood disorder, whereas the RAND-36 emotional well-being scale measures general mood or affect and the MHC also assesses functioning, and (3) there are likely detriments to realms of mental health other than anxiety and depression that are associated with pruritus, and thus were detected by the MHC but not the HADS. For example, the statistically significant and clinically important difference in the social functioning scale of the RAND-36 between the two pruritus groups supports this contention.

A comparison of our RAND-36 data to Canadian normative data for the SF-36 (Hopman *et al*, 2000) shows that mean scale scores of the none-mild pruritus group were lower (4 to 10 points), except for the physical functioning, role physical, and pain scales. For the moderate-severe pruritus group, mean scores were lower (between 9 and 27 points) for all SF-36 scales in comparison to the general Canadian population. It should be noted, however, that the present study did not include subjects over the age of 70, whereas the Canadian normative data includes subjects above this age. In comparison with results from HRQL studies in other chronic disease populations (Erickson *et al*, 2002; Frank *et al*, 2002; Jhingran *et al*, 1996; Revicki *et al*, 1998), the none-mild pruritus group had

mostly higher, with some similar, mean scale scores, whereas the moderate-severe pruritus group had similar or lower mean scale scores.

Overall, although these comparisons must be viewed in light of their inherent limitations, they suggest that patients with chronic plaque psoriasis associated with none-mild pruritus have slightly worse HRQL than the general population but better HRQL than other chronic disease populations. On the other hand, patients with chronic plaque psoriasis associated with moderate-severe pruritus have worse HRQL than the general population and in the range of that of other chronic disease populations.

Interpretations from our study are tempered by three main limitations. Firstly, the cross-sectional design of the study limits the interpretation of the results to an association between pruritus and poorer HRQL; longitudinal studies are required to better determine a causal relationship between the two. Secondly, a large portion of the subjects were recruited from phototherapy clinics; thus, the sample is not fully representative of the population with chronic plaque psoriasis. Light treatment is a time-consuming and demanding therapy that requires dedication and commitment on the part of the patient. It may be that the disease or its symptoms could be more bothersome for phototherapy patients than for patients not undergoing this therapy. Lastly, although the sample size was sufficient to detect a difference in RAND-36 and DLQI scores between the two pruritus groups, numbers may not be sufficient to detect a difference in HADS scores. Thus, further studies addressing pruritus and using the HADS to measure anxiety and depressive symptomatology are indicated.

The results of this study provide novel information in dermatology, specifically the HRQL detriment associated with pruritus as a symptom of chronic plaque psoriasis. To our knowledge, this detriment has not been previously quantified and interpreted for clinical importance. We demonstrate herein that pruritus has a statistically significant and clinically important association with poorer HRQL in patients with chronic plaque psoriasis. The relationship between pruritus and mental health is less clear, however, as we could not demonstrate an association of pruritus severity with the HADS. We contend further research is warranted in this context since the literature suggests pruritus affects mental health and we show herein that pruritus is associated with detriments to emotional well-being as measured by the RAND-36 and with detriments to other realms of mental health, including social functioning.

Based on this study, we conclude that pruritus, which may be underestimated and unaddressed in clinical practice, is a potentially serious and debilitating symptom that warrants medical attention and treatment, and further research investment.

Table 3.1: Demographic Characteristics

		None-Mild Pruritus (N = 84)	Moderate-Severe Pruritus (N = 40)
Age	<30	12 (14.3%)	4 (10.0%)
	30-39	15 (17.9%)	6 (15.0%)
	40-49	12 (14.3%)	10 (25.0%)
	50-59	26 (31.0%)	13 (32.5%)
	60+	19 (22.6%)	7 (17.5%)
Sex*	Male	51 (60.7%)	16 (40.0%)
	Female	33 (39.3%)	24 (60.0%)
Marital Status	Single	21 (25.0%)	8 (20.0%)
	Married/partnership	55 (65.5%)	26 (65.0%)
	Separated/divorced/ widowed	8 (9.5%)	6 (15.0%)
Education	Less than high school/ high school graduate	39 (46.4%)	20 (50.0%)
	College graduate	45 (53.6%)	20 (50.0%)
Main Activity	Working at job	63 (75.0%)	27 (67.5%)
	Looking for work	1 (1.2%)	1 (2.5%)
	Keeping house	6 (7.1%)	1 (2.5%)
	Student	2 (2.4%)	0 (0.0%)
	Unemployed due to disability	2 (2.4%)	6 (15.0%)
	Retired	10 (11.9%)	5 (12.5%)
Income	Under 10,000	3 (3.6%)	4 (10.0%)
	10,000-29,999	7 (8.3%)	5 (12.5%)
	30,000-49,999	18 (21.4%)	8 (20.0%)
	50,000-69,000	15 (17.9%)	9 (22.5%)
	70,000 and above	30 (35.7%)	11 (27.5%)
Ethnic	Caucasian	76 (90.5%)	37 (92.5%)
	Asian/Oriental	4 (4.8%)	1 (2.5%)
	East Indian	2 (2.4%)	1 (2.5%)
	Black	1 (1.2%)	0 (0.0%)
	Native Indian	0 (0.0%)	1 (2.5%)
Comorbidities*		1.40 (SD 1.56)	2.43 (SD 1.75)
SAPASI Score*		9.36 (SD 6.74)	16.00 (SD 13.14)

* $p < 0.05$

Table 3.2: HRQL Scores

	None-Mild Pruritus Group Mean (SD)	Moderate-Severe Pruritus Group Mean (SD)	Unadjusted Mean Difference	Adjusted Mean Difference**
RAND-36				
Physical Functioning	84.76 (21.00)	76.25 (25.74)	-8.51	-0.51
Role - Physical	81.33 (33.32)	60.00 (39.14)	-21.33*	-15.10*
Pain	80.65 (20.86)	57.05 (26.11)	-23.60*	-16.41*
General Health	66.98 (17.95)	55.75 (25.23)	-11.23*	-3.82
Energy/Fatigue	61.19 (18.43)	44.87 (20.76)	-16.32*	-9.37*
Social Functioning	82.29 (21.88)	63.75 (26.52)	-18.54*	-12.09*
Role - Emotional	79.52 (36.38)	56.67 (44.79)	-22.85*	-12.53
Emotion	73.19 (16.98)	60.72 (19.57)	-12.47*	-7.74*
PHC (T-score)	49.08 (9.44)	41.38 (10.60)	-7.70*	-4.33*
MHC (T-score)	47.40 (10.28)	37.97 (11.77)	-9.42*	-5.65*
DLQI	5.54 (4.43)	11.25 (5.33)	5.71*	3.93*

* $p < 0.05$
** Multiple linear regression analyses adjusted for age, sex, marital status, education, number of comorbidities, and SAPASI score

Table 3.3: HADS Scores

	HADS Anxiety	HADS Depression
None-Mild Pruritus Group Mean (SD)	5.73 (3.48)	3.25 (3.28)
Moderate-Severe Pruritus Group Mean (SD)	8.10 (3.99)	4.85 (3.10)
Unadjusted Mean Difference	2.37*	1.60*
Unadjusted Odds Ratio	4.71*	2.16
Unadjusted 95% Confidence Interval	1.687 – 13.174	0.293 – 15.903
Adjusted Odds Ratio**	2.77	0.01
Adjusted 95% Confidence Interval**	0.833 – 9.181	0.000 – 22.183

* $p < 0.05$
** Multiple logistic regression analyses adjusted for age, sex, marital status, education, number of comorbidities, and SAPASI score

Figure 3.1: RAND-36 PHC Summary Scores

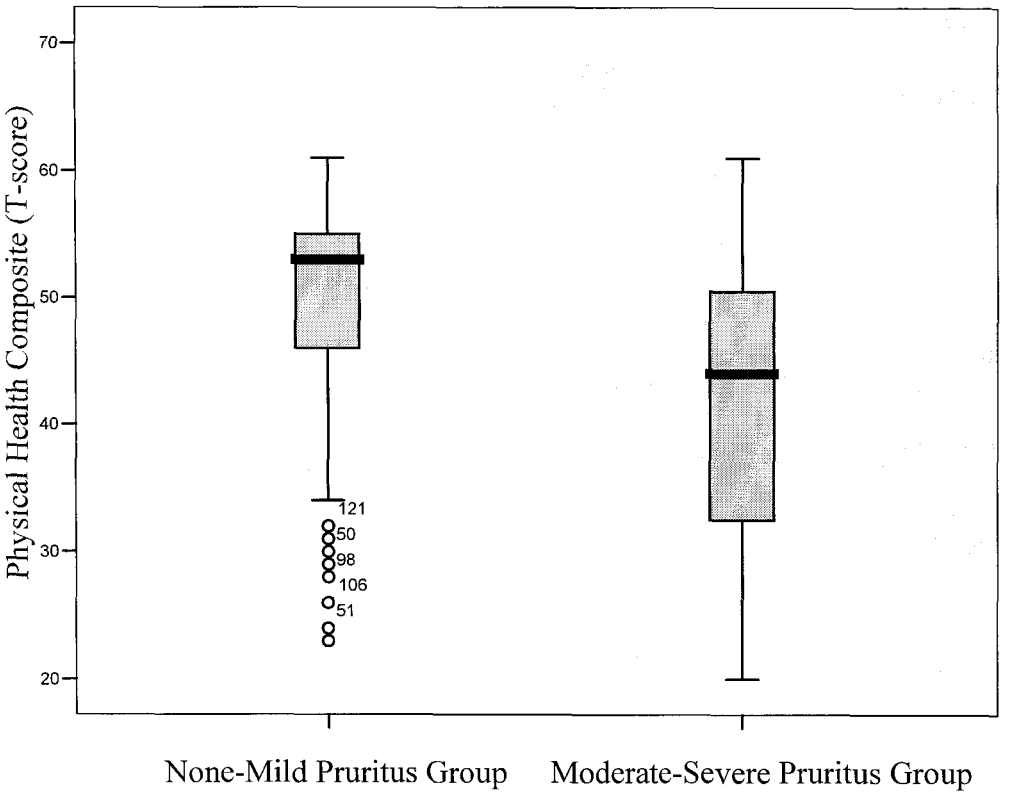


Figure 3.2: RAND-36 MHC Summary Scores

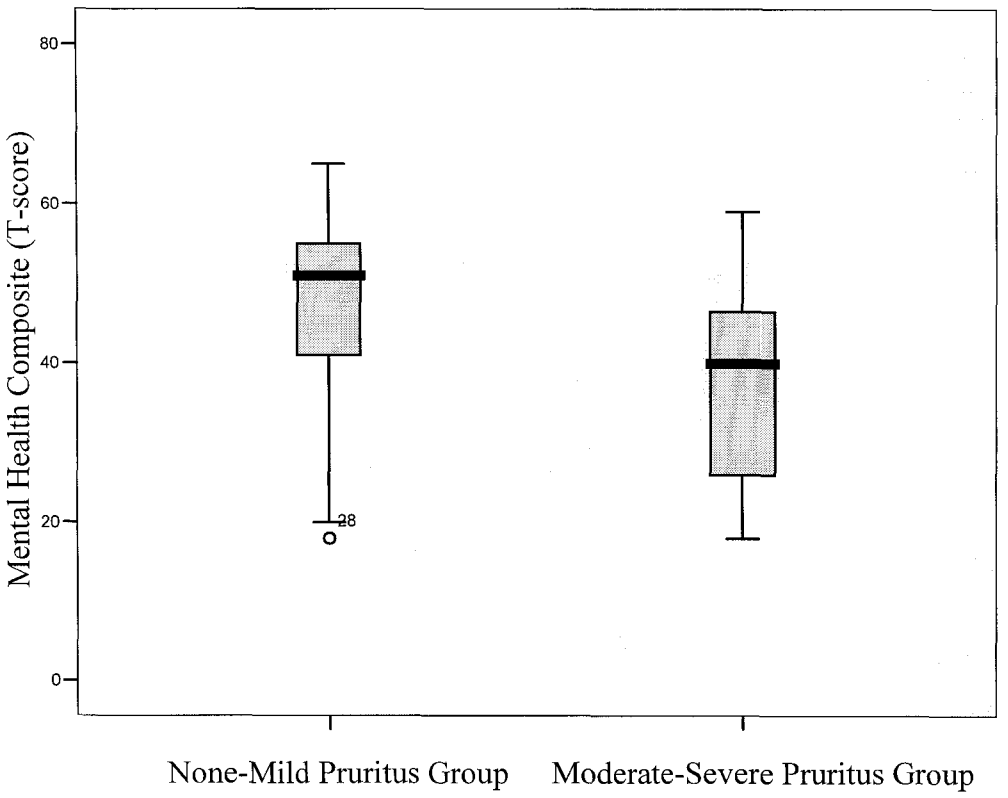


Figure 3.3: DLQI Scores

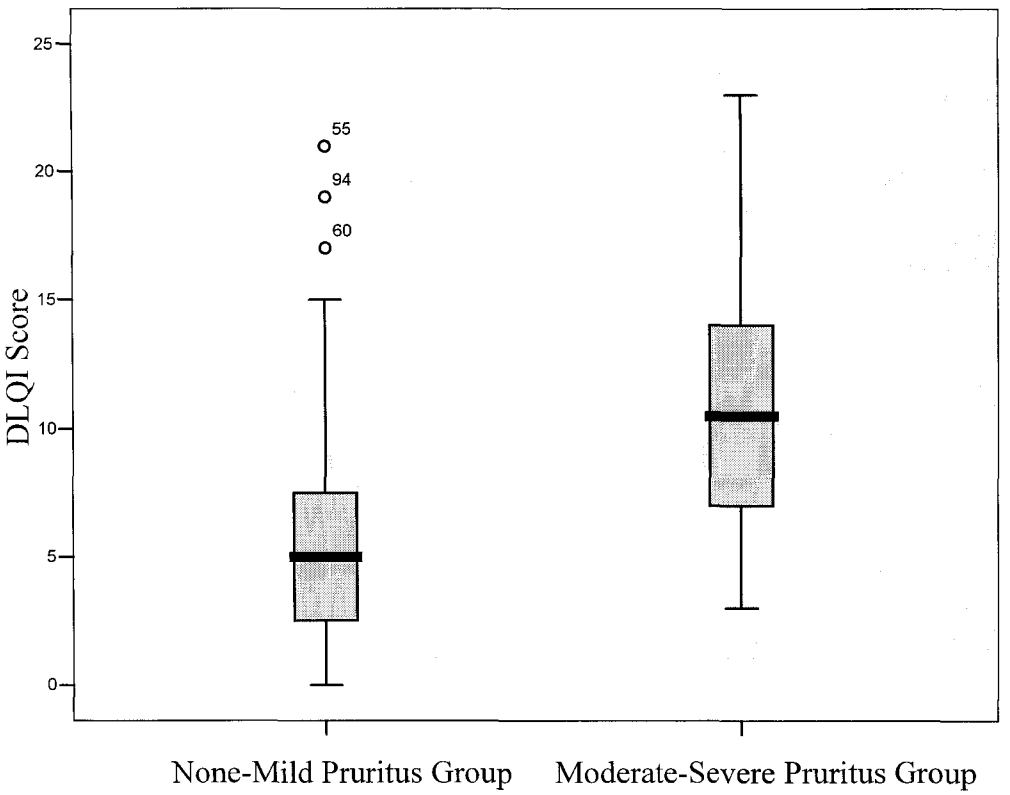


Figure 3.4: HADS Anxiety Subscale Scores

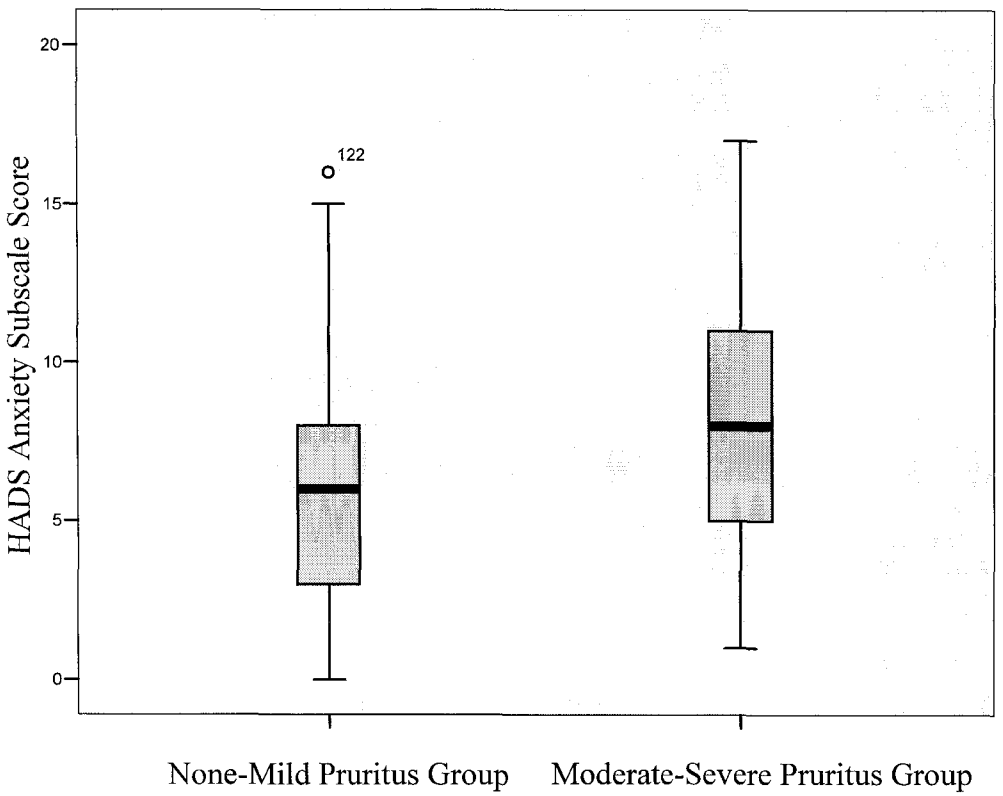
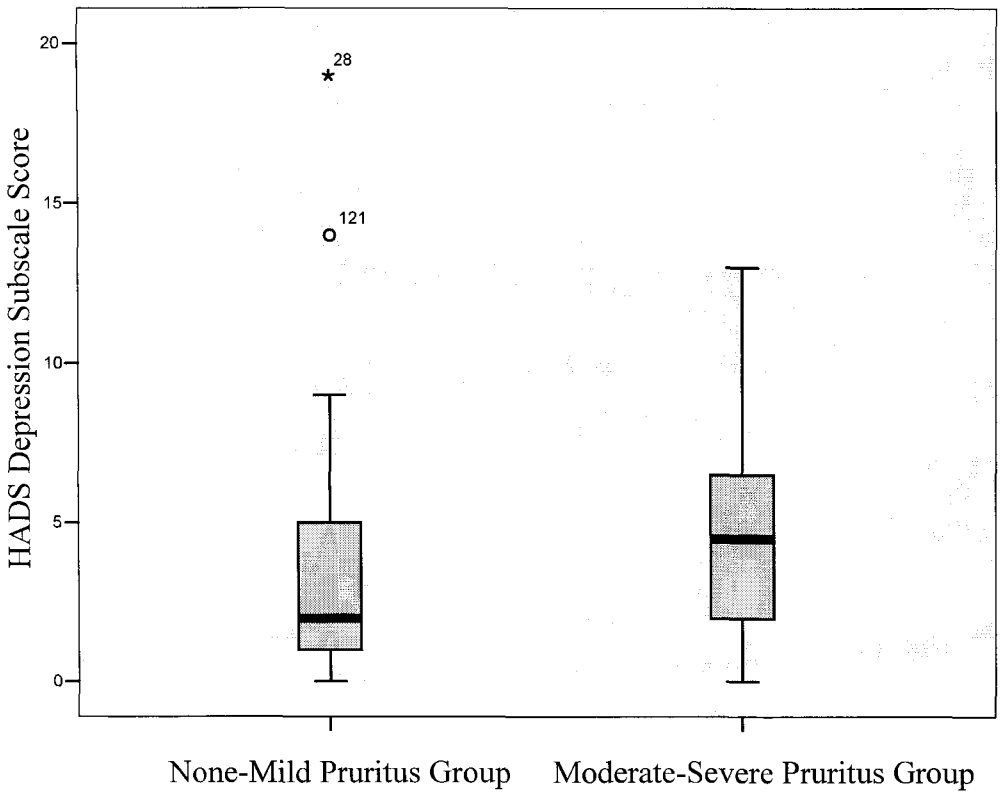


Figure 3.5: HADS Depression Subscale Scores



References

Baker DR: Prioritization of health services: the Oregon Basic Health Services Act and its implications for dermatologists and patients with dermatologic disease. *Dermatol Clin* 11:241-249, 1993

Biringer E, Mykletun A, Dahl AA, Smith AD, Engedal K, Nygaard HA, Lund A: The association between depression, anxiety, and cognitive function in the elderly general population – the Hordaland Health Study. *Int J Geriatr Psychiatry* 20:989-997, 2005

Bjelland I, Dahl AA, Haug TT, Neckelmann D: The validity of the Hospital Anxiety and Depression Scale: An updated literature review. *J Psychosom Res* 52:69-77, 2002

Cunningham WE, Nakazono TT, Tsai KL, Hays RD: Do differences in methods for constructing SF-36 physical and mental health summary measures change their associations with chronic medical conditions and utilization? *Qual Life Res* 12:1029-1035, 2003

Dahl RE, Bernhisel-Broadbent J, Scanlon-Holdford S, Sampsom HA, Lupo M: Sleep disturbances in children with atopic dermatitis. *Arch Pediatr Adolesc Med* 149:856-860, 1995

Duque MI, Yosipovitch G, Chan YH, Smith R, Levy P: Itch, pain, and burning sensation are common symptoms in mild to moderate chronic venous insufficiency with an impact on quality of life. *J Am Acad Dermatol* 53:504-508, 2005

Erickson SR, Christian RD Jr, Kirking DM, Halman LJ: Relationship between patient and disease characteristics, and health-related quality of life in adults with asthma. *Respir Med* 96:450-460, 2002

Feldman SR, Fleischer AB Jr, Reboussin DM, Rapp SR, Exum ML, Clark AR, Nurre L: The self-administered psoriasis area and severity index is valid and reliable. *J Invest Dermatol* 106:183-186, 1996

Finlay AY, Khan GK: Dermatology Life Quality Index (DLQI) – A simple practical measure for routine clinical use. *Clin Exp Dermatol* 19:210-216, 1994

Finlay AY, Khan GK: Dermatology Life Quality Index: Information and conditions concerning use. URL: www.dermatology.org.uk/portal/quality/dlqiinstruc.html (Accessed 12/12/2005)

Fleischer AB Jr., Rapp SR, Reboussin DM, Vanarthos JC, Feldman SR: Patient measurement of psoriasis disease severity with a structured instrument. *J Invest Dermatol* 102:967-969, 1994

Frank L, Kleinman L, Rentz A, Ciesla G, Kim JJ, Zacker C: Health-related quality of life associated with irritable bowel syndrome: Comparison with other chronic diseases. *Clin Ther* 24:675-689, 2002

Gilchrest BA: Cutaneous sensation and pathophysiology of pruritus. In: *Pathophysiology of Dermatologic Diseases*. Soter NA, Baden HP (eds). New York: McGraw-Hill, 1984, p 73-80

Gupta MA, Gupta AK, Kirkby S, *et al*: Pruritus in psoriasis: A prospective study of some psychiatric and dermatologic correlates. *Arch Dermatol* 124:1052-1057, 1988

Gupta MA, Gupta AK, Schork NJ, Ellis CN: Depression modulates pruritus perception: A study of pruritus in psoriasis, atopic dermatitis, and chronic idiopathic urticaria. *Psychosom Med* 56:36-40, 1994

Hays RD: *RAND-36 Health Status Inventory*. San Antonio: The Psychological Corporation, 1998.

Herrmann C: International experiences with the Hospital Anxiety and Depression Scale – A review of validation data and clinical results. *J Psychosom Res* 42:17-41, 1997

Hongbo Y, Thomas CL, Harrison MA, Salek MS, Finlay AY: Translating the science of quality of life into practice: What do Dermatology Life Quality Index scores mean? *J Invest Dermatol* 125:659-664, 2005

Hopman WM, Towheed T, Anastassiades T, *et al*: Canadian normative data for the SF-36 health survey. *CMAJ* 163:265-271, 2000

Jhingran P, Cady RK, Rubino J, Miller D, Grice RB, Gutterman DL: Improvements in health-related quality of life with sumatriptan treatment for migraine. *J Fam Pract* 42:36-42, 1996

Johnson JA, Maddigan SL: Performance of the RAND-12 and SF-12 summary scores in type 2 diabetes. *Qual Life Res* 13:449-456, 2004

Krueger G, Koo J, Lebwohl M, Menter A, Stern RS, Rolstad T: The impact of psoriasis on quality of life: Results of a 1998 National Psoriasis Foundation patient-membership survey. *Arch Dermatol* 137:280-284, 2001

Lewis V, Finlay AY: 10 years experience of the Dermatology Life Quality Index (DLQI). *J Investig Dermatol Symp Proc* 9:169-180, 2004

Moloney FJ, Keane S, O'Kelly P, Conlon PJ, Murphy GM: The impact of skin disease following renal transplantation on quality of life. *Br J Dermatol* 153:574-578, 2005

Picardi A, Abeni D, Melchi CF, Puddu P, Pasquini P: Psychiatric morbidity in dermatological outpatients: An issue to be recognized. *Br J Dermatol* 143:983-991, 2000

Revicki DA, Wood M, Maton PN, Sorensen S: The impact of gastroesophageal reflux disease on health-related quality of life. *Am J Med* 104:252-258, 1998

Russell PS: Dermatology in the Oregon Plan with implications for health care plans in other states. *Arch Dermatol* 130:709-712, 1994

Sampogna F, Picardi A, Melchi CF, Pasquini P, Abeni D: The impact of skin disease on patients: Comparing dermatologists' opinions with research data collected on their patients. *Br J Dermatol* 148:989-995, 2003

Sampogna F, Sera F, Mazzotti E, Pasquini P, Picardi A, Abeni D, IMPROVE Study Group: Performance of the self-administered psoriasis area and severity index in evaluating clinical and sociodemographic subgroups of patients with psoriasis. *Arch Dermatol* 139:353-358, 2003

Samsa G, Edelman D, Rothman ML, Williams GR, Lipscomb J, Matchar D: Determining clinically important differences in health status measures: a general approach with illustration to the Health Utilities Index Mark II. *Pharmacoeconomics* 15:141-155, 1999

Simon GE, Revicki DA, Grothaus L, Vonkorff M: SF-36 summary scores: Are physical and mental health truly distinct? *Med Care* 36:567-572, 1998

Stewart AL, Greenfield S, Hays RD, *et al*: Functional status and well-being of patients with chronic conditions: Results from the Medical Outcomes Study. *JAMA* 262:907-913, 1989

Stores G, Burrows A, Crawford C: Physiological sleep disturbance in children with atopic dermatitis: A case control study. *Pediatr Dermatol* 15:264-268, 1998

Szepietowski JC, Reich A, Wisnicka B: Pruritus and psoriasis. *Br J Dermatol* 151:1284, 2004

Taft C, Karlsson J, Sullivan M: Do SF-36 summary component scores accurately summarize subscale scores? *Qual Life Res* 10:395-404, 2001

Weinberger M, Kirkman MS, Samsa GP, Cowper PA, Shortliffe EA, Simel DL, Feussner JR: The relationship between glycemic control and health-related quality of life in patients with non-insulin-dependent diabetes mellitus. *Med Care* 32:1173-1181, 1994

Yosipovitch G, Goon A, Wee J, Chan YH, Goh CL: The prevalence and clinical characteristics of pruritus among patients with extensive psoriasis. *Br J Dermatol* 143:969-973, 2000

Yosipovitch G, Zucker I, Boner G, Gafter U, Shapira Y, David M: A questionnaire for the assessment of pruritus: Validation in uremic patients. *Acta Derm Venereol* 81:108-111, 2001

Younossi ZM, Kiwi ML, Boparai N, Price LL, Guyatt G: Cholestatic liver diseases and health-related quality of life. *Am J Gastroenterol* 95:497-502, 2000

Zigmond AS, Snaith RP: The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 67:361-370, 1983

Chapter 4

General Discussion and Conclusion

Pruritus is a common and potentially debilitating symptom associated with considerable psychiatric morbidity (Gupta *et al*, 1988; Picardi *et al*, 2000; Sampogna *et al*, 2003), sleep disturbances (Dahl *et al*, 1995; Stores *et al*, 1998; Yosipovitch *et al*, 2000), and an overall reduced health-related quality of life (HRQL) (Duque *et al*, 2005; Moloney *et al*, 2005; Sampogna *et al*, 2003; Younossi *et al*, 2000). However, there is minimal literature evaluating the overall effect of pruritus on HRQL. An appreciation of the need for expanded studies addressing mental well-being and measurement of HRQL in patients with pruritus provides the impetus for a study to quantify and interpret for clinical importance the association between pruritus severity and HRQL, anxiety, and depressive symptomatology.

However, the accurate assessment of these associations, particularly for a subjective sensory symptom like pruritus, requires methods to accurately measure symptom severity from a patient perspective. Currently available methods to measure pruritus intensity, including techniques that record scratching movements and subjective assessments that make use of scales (Hagermark and Wahlgren, 1992), may not be suitable to measure the severity of pruritus, because intensity is only one facet of this multidimensional symptom. Two instruments for the characterization and evaluation of pruritus have recently been developed based on the long (Darsow *et al*, 2001) and short (Yosipovitch *et al*, 2001) forms of the McGill Pain Questionnaire (Melzack, 1975), but neither quantifies

pruritus severity specifically, nor patient burden generally. Thus, we contend that the development of a practical questionnaire assessing pruritus severity and resulting patient burden is required for both clinical evaluation and research.

The objectives of this study were threefold: (1) to develop a self-report questionnaire to quantify pruritus severity and provide evidence of its validity and reliability, (2) to measure and compare the HRQL of patients with chronic plaque psoriasis associated with varying levels of pruritus, and (3) to measure and compare levels of anxiety and depressive symptomatology in patients with chronic plaque psoriasis associated with varying levels of pruritus.

For the first objective, an interviewer-administered instrument developed by Yosipovitch *et al* was modified to provide a self-report format. Yosipovitch's instrument was developed for the characterization and evaluation of pruritus, but has no method of scoring with which to quantify severity of the symptom. The modified pruritus questionnaire was completed, along with the RAND-36 Health Status Inventory and Dermatology Life Quality Index (DLQI), by 93 subjects with psoriasis-associated pruritus recruited from phototherapy and dermatology clinics in Alberta. Items were selected from the modified pruritus questionnaire for the novel questionnaire, the Itch Severity Scale (ISS), based on exploratory factor analysis, studies of internal consistency, inter-item correlation analyses, and correlation analyses with HRQL scores. Seven of the initial 11 candidate items were retained for inclusion in the new questionnaire: item 3 (itch description B), item 4 (frequency), item 6 (effect on sleep), item 7 (effect on mood),

item 8 (effect on sexual desire/function), item 9 (itch intensity using 5-point Likert scale), and item 11 (body surface area involved).

The ISS was assessed for construct validity through correlations with three HRQL scores: ISS scores moderately correlated with physical health composite (PHC) and mental health composite (MHC) scores of the RAND-36 and strongly correlated with DLQI scores.

We also observed good evidence of reliability for the new instrument. Internal consistency reliability of the ISS was above the minimum acceptable value for group-level comparison. Thirteen subjects completed the modified pruritus questionnaire approximately two weeks following initial questionnaire completion, to estimate test-retest reliability of the ISS. From this, we observed test-retest reliability well above the minimum acceptable value for group-level comparison and suggestive of sufficient reliability for individual comparisons.

For the second and third objectives, subjects with chronic plaque psoriasis recruited from phototherapy and dermatology clinics in Alberta completed a questionnaire package that included questions on demographics and comorbidities, a Self-Administered Psoriasis Area and Severity Index (SAPASI), the aforementioned modified pruritus questionnaire, RAND-36, DLQI, and Hospital Anxiety and Depression Scale (HADS). ISS scores were calculated based on responses to the modified pruritus questionnaire. Subjects were classified into two groups based on ISS scores using a median split. The none-mild

pruritus group (N = 84) consisted of subjects with ISS scores below the median, including those reporting no pruritus. The moderate-severe pruritus group (N = 40) consisted of subjects with ISS scores above the median.

After adjusting for age, sex, marital status, education, number of comorbidities, and SAPASI score, multiple linear regression analyses showed clinically important mean differences in all scales of the RAND-36, with the exception of physical functioning, between the none-mild and moderate-severe pruritus groups. Differences were statistically significant in the role-physical, pain, energy/fatigue, social functioning, and emotional well-being scales. Mean differences in RAND-36 summary scores (PHC and MHC) were both statistically significant and clinically important. Moreover, the mean difference in DLQI scores between the two pruritus groups was also statistically significant and clinically important, after adjusting for the same potential confounders.

Multiple logistic regression analyses showed no significant differences in likelihood of having anxiety or depression as measured by the HADS between the none-mild and moderate-severe pruritus groups, after adjusting for potential confounders. Although no association was found between pruritus and HADS scores in this study, literature suggests that pruritus has a considerable association with mental health. Moreover, data from this study suggests that pruritus had a statistically significant and clinically important association with mental health as measured by the RAND-36.

Possible explanations for the lack of a significant association between pruritus and HADS scores in spite of the presence of a significant association between pruritus and both the emotional well-being scale and MHC of the RAND-36 include the following: (1) the sample size was not large enough to detect a difference with the HADS, (2) the measurements are strategically different as the HADS addresses only the psychic symptoms of neurosis to diagnose mood disorder whereas the emotional well-being scale measures general mood or affect and the MHC also assesses functioning, and (3) there are likely detriments to aspects of mental health other than anxiety and depression that are associated with pruritus, and thus were detected by the MHC but not the HADS. For example, the statistically significant and clinically important difference in the social functioning scale of the RAND-36 between the two pruritus groups supports this contention.

There are two main future directions for this research. First, since an accumulation of validity and reliability evidence is important to increase confidence that a measure is appropriate, further studies are required to add to the validity and reliability evidence of the ISS in other samples and clinics. Additional evidence of validity should include responsiveness of the ISS to change, as one desired function of the ISS is to assess treatment effectiveness. It is also important for further studies to determine the test-retest reliability of the ISS since this study only estimated test-retest reliability based on responses to the modified pruritus questionnaire. Moreover, a clinically important difference in ISS scores may be reassessed to confirm or refute the clinically important difference calculated in this sample. Ideally, this would include assessments of clinically

important changes in pruritus severity in longitudinal studies. Second, due to the cross-sectional nature of this research, current interpretation is limited to the question of an association between pruritus and HRQL. Longitudinal studies are required to determine a causal relationship between the two. This could include, for example, using a treatment for pruritus of known efficacy and comparing HRQL before and after treatment intervention.

In summary, this research has contributed to the field of dermatology in two ways. First, we developed, to our knowledge, the first questionnaire for the quantification of pruritus severity, the Itch Severity Scale. Results provide preliminary evidence of its validity and reliability. Its self-report nature and short time for completion make it practical, convenient and applicable for use in the clinic and through the mail. Such an instrument may be useful to compare pruritus severity among different disease populations. This is important to increase the awareness of health professionals regarding which diseases are pruritic and the general severity of the pruritus to promote addressing the symptom in medical practice. Such an instrument may also be useful to assess the effectiveness of treatments for pruritus. It is more convenient and less time-consuming than recording scratching movements, and more accurate than measuring solely intensity via self-report scales (e.g., visual analogue scale) or using a non-pruritus specific measure of HRQL.

Second, we used the ISS to gauge symptom severity in order to quantify and interpret clinically important HRQL decrements associated with pruritus as a symptom of disease. To our knowledge, this quantification and interpretation has not been previously studied.

We demonstrated that pruritus severity has a statistically significant and clinically important association with poorer HRQL in patients with chronic plaque psoriasis as measured by the RAND-36 and DLQI. The relationship between pruritus and mental health is less clear, however, as we could not demonstrate an association of pruritus severity with the HADS. Further research is warranted in this context since our findings are not in keeping with previous literature suggesting pruritus affects mental health. Further, we observed that pruritus is associated with detriments to emotional well-being as measured by the RAND-36 and with detriments to other realms of mental health, including social functioning.

Based on this study, we conclude that pruritus, which may be underestimated and unaddressed in clinical practice, is a potentially serious and debilitating symptom that warrants medical attention and treatment, and further research investment.

References

Dahl RE, Bernhisel-Broadbent J, Scanlon-Holdford S, Sampsom HA, Lupo M: Sleep disturbances in children with atopic dermatitis. *Arch Pediatr Adolesc Med* 149:856-860, 1995

Darsow U, Scharein E, Simon D, Walter G, Bromm B, Ring J: New aspects of itch pathophysiology: Component analysis of atopic itch using the 'Eppendorf Itch Questionnaire'. *Int Arch Allergy Immunol* 124:326-331, 2001

Duque MI, Yosipovitch G, Chan YH, Smith R, Levy P: Itch, pain, and burning sensation are common symptoms in mild to moderate chronic venous insufficiency with an impact on quality of life. *J Am Acad Dermatol* 53:504-508, 2005

Gupta MA, Gupta AK, Kirkby S, *et al*: Pruritus in psoriasis: A prospective study of some psychiatric and dermatologic correlates. *Arch Dermatol* 124:1052-1057, 1988

Hagermark O, Wahlgren CF: Some methods for evaluating clinical itch and their application for studying pathophysiological mechanisms. *J Dermatol Sci* 4:55-62, 1992

Melzack R. The McGill Pain Questionnaire: Major properties and scoring methods. *Pain* 1:277-299, 1975

Moloney FJ, Keane S, O'Kelly P, Conlon PJ, Murphy GM: The impact of skin disease following renal transplantation on quality of life. *Br J Dermatol* 153:574-578, 2005

Picardi A, Abeni D, Melchi CF, Puddu P, Pasquini P: Psychiatric morbidity in dermatological outpatients: An issue to be recognized. *Br J Dermatol* 143:983-991, 2000

Sampogna F, Picardi A, Melchi CF, Pasquini P, Abeni D: The impact of skin disease on patients: Comparing dermatologists' opinions with research data collected on their patients. *Br J Dermatol* 148:989-995, 2003

Stores G, Burrows A, Crawford C: Physiological sleep disturbance in children with atopic dermatitis: A case control study. *Pediatr Dermatol* 15:264-268, 1998

Yosipovitch G, Goon A, Wee J, Chan YH, Goh CL: The prevalence and clinical characteristics of pruritus among patients with extensive psoriasis. *Br J Dermatol* 143:969-973, 2000

Yosipovitch G, Zucker I, Boner G, Gafter U, Shapira Y, David M: A questionnaire for the assessment of pruritus: Validation in uremic patients. *Acta Derm Venereol* 81:108-111, 2001

Younossi ZM, Kiwi ML, Boparai N, Price LL, Guyatt G: Cholestatic liver diseases and health-related quality of life. *Am J Gastroenterol* 95:497-502, 2000

Appendix A

Questionnaire Package

Date: _____

PERSONAL INFORMATION

The following questions are meant to help us describe the results of this research. Please put an 'X' on the line that corresponds to your answer.

1. How old are you?	< 30 years old	1_____
	30-39 years old	2_____
	40-49 years old	3_____
	50-59 years old	4_____
	60 or more years old	5_____
2. Are you:	Male	1_____
	Female	2_____
3. Are you currently:	Single	1_____
	Married/In a partnership	2_____
	Separated/Divorced	3_____
	Widowed	4_____

4. What is the highest level of education you have completed?

Less than high school	1_____
High school graduate	2_____
College or University graduate	3_____

5. During the past 12 months, what best describes your main activity?

Working at a job or business	1_____
Looking for work	2_____
Keeping house	3_____
A student	4_____
Unemployed due to disability	5_____
Retired	6_____

6. Which of the following categories includes your total household income (before taxes) in the last tax year?

Under $10,000	1_____
$10,000 - $29,999	2_____
$30,000 - $49,999	3_____
$50,000 - $69,999	4_____
$70,000 and above	5_____

7. What is your ethnic background?

Caucasian	1_____
Asian/Oriental	2_____
East Indian	3_____
Black	4_____
Native Indian	5_____
Other (please specify below)	6_____

_____

MEDICAL BACKGROUND

1. Have you ever been told by a health professional that you have:
(please circle Yes or No)

a. Asthma	Yes	No
b. Arthritis or rheumatism	Yes	No
c. Back problems, excluding arthritis	Yes	No
d. High blood pressure	Yes	No
e. Diabetes	Yes	No
f. Migraine headaches	Yes	No
g. Chronic bronchitis or emphysema	Yes	No
h. Sinusitis	Yes	No
i. Epilepsy	Yes	No
j. Heart disease or had a heart attack	Yes	No
k. Stroke	Yes	No
l. Cancer	Yes	No
m. Stomach or intestinal ulcers	Yes	No
n. Urinary incontinence	Yes	No
o. A bowel disorder (Crohn's or colitis)	Yes	No
p. Glaucoma	Yes	No
q. A thyroid condition	Yes	No

r. Other, please specify:

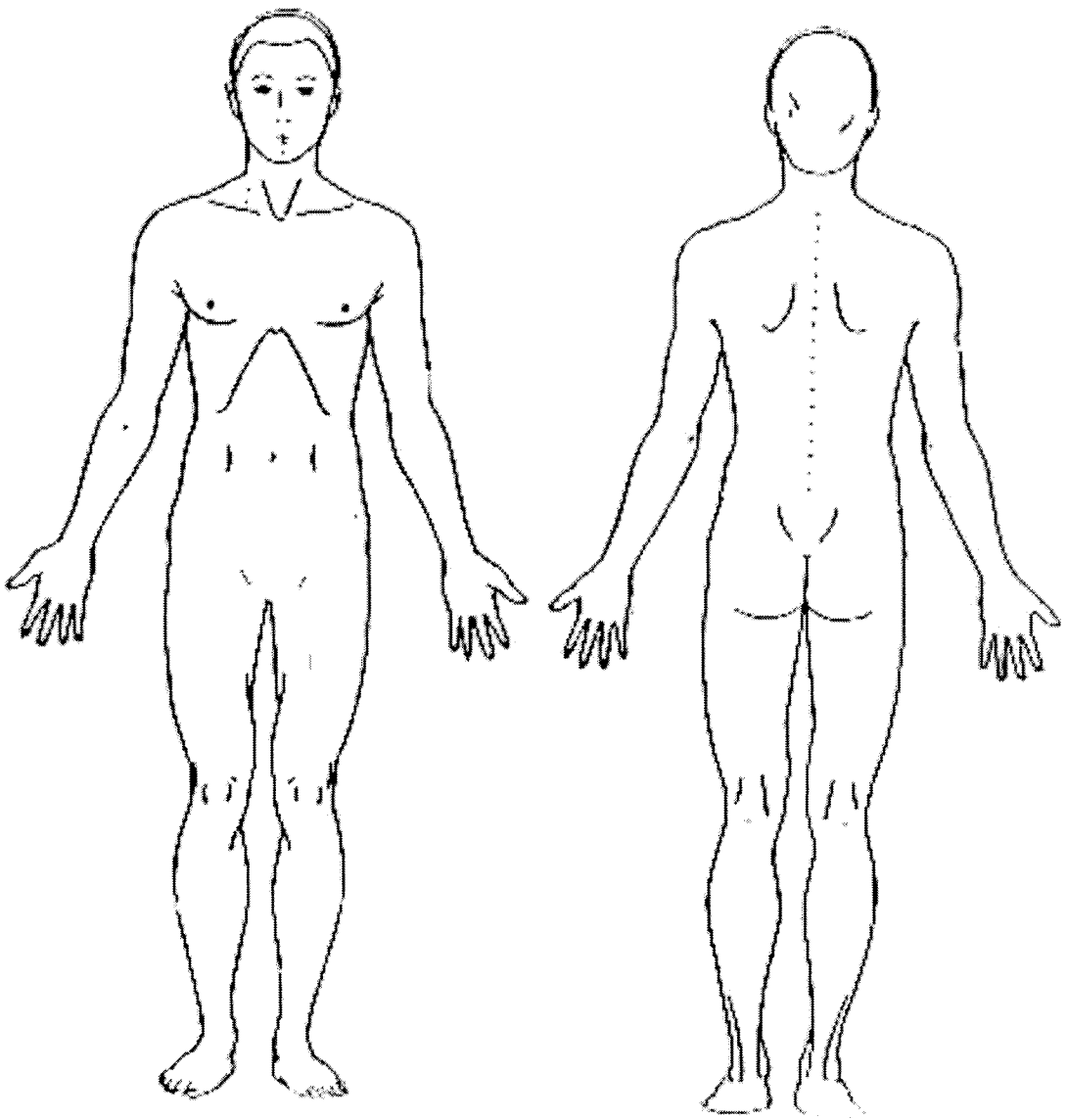
2. What medications are you currently using? _____

_____

ABOUT YOUR PSORIASIS

1. How long have you had psoriasis? _____

2. On the diagram below, please shade in the areas currently affected by psoriasis.



3. How would you describe your "average" psoriatic lesion (please mark on the lines below with an 'X').

No redness	Slight pink	Pink	Red	Dark red

No thickness	Feels firm	Raised	Thick	Very thick

No scale	Slight scale	Scaly	Flaky	Very flaky

4. Overall, how would you rate your psoriasis (please mark on the line below with an 'X')?

No psoriasis	Severe psoriasis

Questions 2 and 3:
Self-Administered Psoriasis Area and Severity Index. Fleischer AB *et al*, 1994. This must not be copied without the permission of the authors.

ABOUT YOUR ITCH

If you have had itch associated with your psoriasis for at least 6 weeks, please answer the following questions to the best of your ability. If you do not have itch associated your psoriasis, you may skip these and go on to the next set of questions (page 82).

1. How long have you had itch associated with your psoriasis? _____

2. How many days of the week are you itchy (please put an 'X' on the line that corresponds to your answer)?

1 – 2 days	1_____
3 – 4 days	2_____
5 – 6 days	3_____
7 days	4_____

3. How many hours per day are you itchy (please put an 'X' on the line that corresponds to your answer)?

<1 hour	1_____
1 – 4 hours	2_____
5 – 8 hours	3_____
9 – 12 hours	4_____
13 – 16 hours	5_____
17 – 20 hours	6_____
>20 hours	7_____

4. Do any of the following symptoms accompany the itch (please circle Yes or No)?

Pain in the itchy area	Yes	No
Sweating	Yes	No
Headache	Yes	No
Heat sensation	Yes	No
Cold sensation	Yes	No
Other _____		

5. Are you currently on any treatments for the itch? Which one(s)? _____

_____

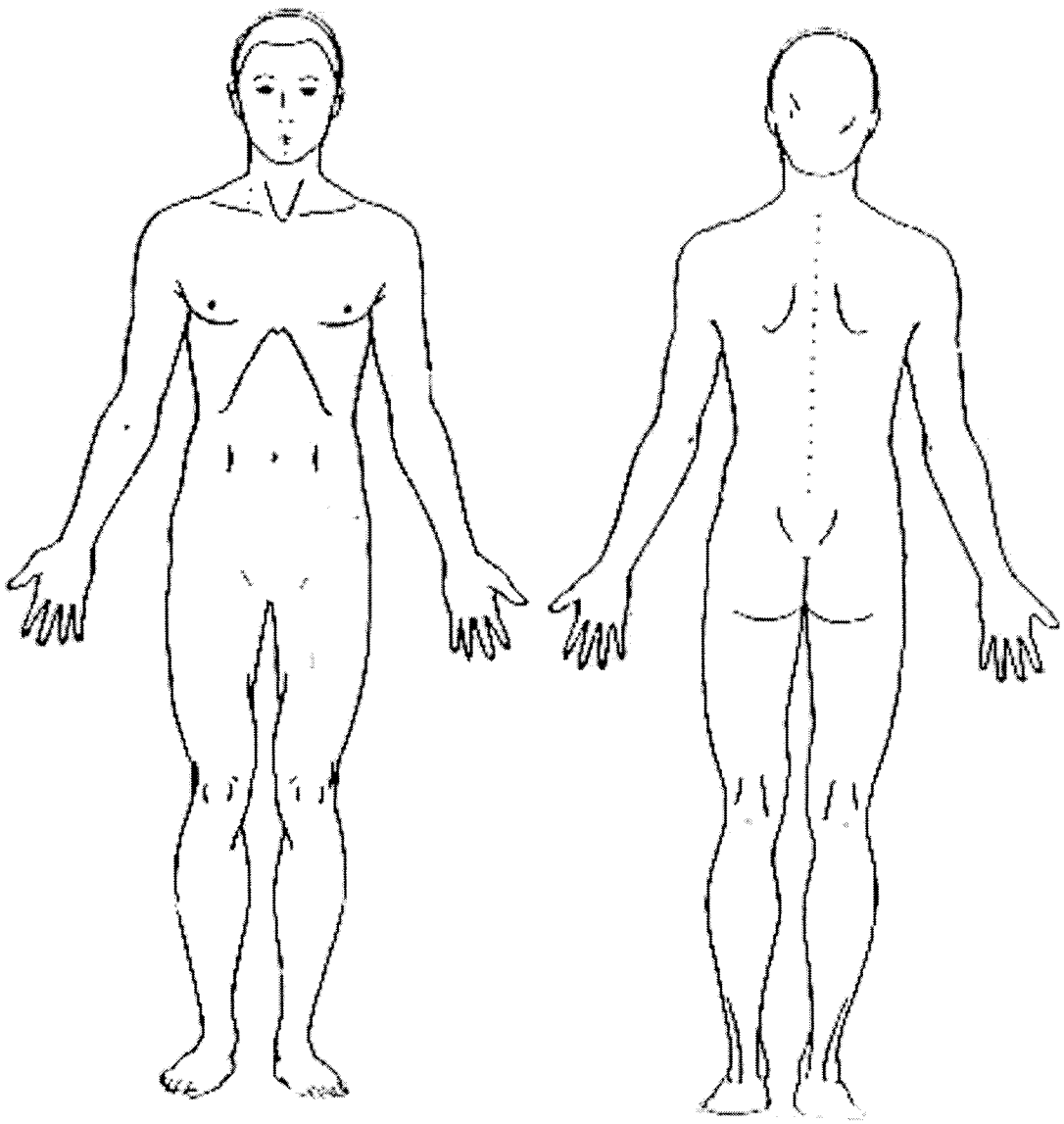
6. Does the treatment make the itch go away (please circle one)?

a. No, it has no effect on the itch

b. It makes the itch go away for a short period of time (less than 24 hours)

c. It makes the itch go away for a long period of time (more than 24 hours)

7. Please shade in the areas where you tend to be itchy.



8. To what extent do the each of the following describe the itch (please put an 'X' in the box that corresponds with your answer):

	not at all	to a small extent	to a moderate extent	to a great extent
Tickling				
Stinging				
Crawling (like ants)				
Stabbing				
Pinching				
Burning				
Bothersome				
Annoying				
Unbearable				
Worrisome				

9. For each part of the day, what is the frequency of appearance of the itch (please put an 'X' in the box that corresponds with your answer)?

	Never itchy	Occasionally itchy	Often itchy	Always itchy
Morning				
Noon				
Evening				
Night				

10. For each part of the day, what is the time-pattern of the itch (please put an 'X' in the box that corresponds with your answer)?

	Continuous	Episodic	Momentary
Morning			
Noon			
Evening			
Night			

11. Please indicate how often any of the following happens (please put an 'X' in the box that corresponds with your answer):

	Almost always	Sometimes	Never
Difficulty falling asleep due to itch			
Awakening due to itch			
Use of sleep medications			

12. Please indicate how each of the following items affects the itch by putting the letter corresponding to your answer (a, b, or c) in the box:

a. Increases
b. Does not affect
c. Relieves

Sleep		Hot Water	
Rest		Cold Water	
Activity		Dryness	
Lying		Sweat	
Sitting		Cold	
Stress		Heat	
Fatigue		Physical Effort	
Eating		Specific Fabrics	

13. Has your mood changed because of the itch (you may circle more than one answer)?

a. No change
b. Depressed
c. More agitated
d. Difficulty in concentration
e. Anxious
f. Other (please specify): _____

14. For the following 4 questions, please put an 'X' on the line that corresponds to your answer.

i) Have your eating habits changed because of the itch? Yes 1_____
No 2_____

ii) Did you start a special diet because of the itch? Yes 1_____
No 2_____

iii) How has itch affected your sexual desire?
Increase in sexual desire 1_____
No change in sexual desire 2_____
Decrease in sexual desire 3_____

iv) How has itch affected your sexual function?
Increase in sexual function 1_____
No change in sexual function 2_____
Decrease in sexual function 3_____

15. Please indicate the intensity of itch for each of the following (please put an 'X' in the box that corresponds with your answer):

	None	Weak	Moderate	Strong	Very strong
Itch in its average state					
Itch in its worst state					
Itch in its best state					
Itch after a mosquito bite					

16. What is the intensity of itching that you experience in each of the following states (please mark on the lines below with an 'X'):

i) Itch in its average state

None Very strong

ii) Itch in its worst state

None Very strong

iii) Itch in its best state

None Very strong

iv) Itch after a mosquito bite

None Very strong

17. Did you find a way to relieve your itch? Yes No

How? _____

18. What do you scratch with (eg. hands, legs, brush, etc.)? _____

_____

RAND-36 HEALTH STATUS INVENTORY

The following questions ask for your views about your health, how you feel and how well you are able to do your usual activities. If you are unsure about how to answer any questions, please give the best answer you can.

Please put an 'X' on the line that corresponds with your answer, unless otherwise specified.

1. In general, would you say your health is:

Excellent	1_____
Very good	2_____
Good	3_____
Fair	4_____
Poor	5_____

2. **Compared to one year ago,** how would you rate your health in general **now**?

Much better now than one year ago	1_____
Somewhat better now than one year ago	2_____
About the same as one year ago	3_____
Somewhat worse now than one year ago	4_____
Much worse now than one year ago	5_____

3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
a. Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports	1_____	2_____	3_____
b. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling or playing golf	1_____	2_____	3_____

	Yes, limited a lot	Yes, limited a little	No, not limited at all
c. Lifting or carrying groceries	1_____	2_____	3_____
d. Climbing **several** flights of stairs	1_____	2_____	3_____
e. Climbing **one** flight of stairs	1_____	2_____	3_____
f. Bending, kneeling or stooping	1_____	2_____	3_____
g. Walking **more than a mile**	1_____	2_____	3_____
h. Walking **several blocks**	1_____	2_____	3_____
i. Walking **one block**	1_____	2_____	3_____
j. Bathing or dressing yourself	1_____	2_____	3_____

4. During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of your physical health**? (please circle Yes or No)

a. Cut down on the **amount of time** you spent on work or other activities	Yes	No
b. **Accomplished less** than you would like	Yes	No
c. Were limited in the **kind** of work or other activities	Yes	No
d. Had **difficulty** performing the work or other activities (for example, it took extra effort)	Yes	No

5. During the **past 4 weeks**, have you had any of the following problems with your work or other regular daily activities **as a result of any emotional problems** (such as feeling depressed or anxious)? (please circle Yes or No)

a. Cut down on the **amount of time** you spent on work or other activities	Yes	No
b. **Accomplished less** than you would like	Yes	No
c. Didn't do work or other activities as **carefully** as usual	Yes	No

6. During the **past 4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbors or groups?

Not at all	1_____
Slightly	2_____
Moderately	3_____
Quite a bit	4_____
Extremely	5_____

7. How much **bodily** pain have you had during the **past 4 weeks**?

None	1_____
Very mild	2_____
Mild	3_____
Moderate	4_____
Severe	5_____
Very severe	6_____

8. During the **past 4 weeks**, how much did **pain** interfere with your normal work (including work both outside the home and housework)?

Not at all	1_____
A little bit	2_____
Moderately	3_____
Quite a bit	4_____
Extremely	5_____

9. These questions are about how you feel and how things have been with you **during the past 4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during **the past 4 weeks**:

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
a. Did you feel full of life?	1	2	3	4	5	6
b. Have you been a very nervous person?	1	2	3	4	5	6
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
d. Have you felt calm and peaceful?	1	2	3	4	5	6
e. Did you have a lot of energy?	1	2	3	4	5	6
f. Have you felt downhearted and blue?	1	2	3	4	5	6
g. Did you feel worn out?	1	2	3	4	5	6
h. Have you been a happy person?	1	2	3	4	5	6
i. Did you feel tired?	1	2	3	4	5	6

10. During the **past 4 weeks**, how much of the time has your **physical health or emotional problems** interfered with your social activities (like visiting with friends, relatives, etc.)?

All of the time	1_____
Most of the time	2_____
Some of the time	3_____
A little of the time	4_____
None of the time	5_____

11. Please choose the answer that best describes how **true** or **false** each of the following statements is for you.

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
a. I seem to get sick a little easier than other people	1_____	2_____	3_____	4_____	5_____
b. I am as healthy as anybody I know	1_____	2_____	3_____	4_____	5_____
c. I expect my health to get worse	1_____	2_____	3_____	4_____	5_____
d. My health is excellent	1_____	2_____	3_____	4_____	5_____

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HOSPITAL ANXIETY AND DEPRESSION SCALE

Please read each item below and circle the reply which comes closest to how you have been feeling in the past week.

Don't take too long over your replies, your immediate reaction to each item will probably be more accurate than a long, thought-out response.

1. I feel tense or 'wound up'

Most of the time

A lot of the time

From time to time, occasionally

Not at all

2. I feel as if I am slowed down

Nearly all the time

Very often

Sometimes

Not at all

3. I still enjoy the things I used to enjoy

Definitely as much

Not quite so much

Only a little

Hardly at all

4. I get a sort of frightened feeling like 'butterflies' in the stomach

Not at all

Occasionally

Quite often

Very often

5. I get a sort of frightened feeling as if something awful is about to happen

Very definitely and quite badly

Yes, but not too badly

A little, but it doesn't worry me

Not at all

6. I have lost interest in my appearance

Definitely

I don't take as much care as I should

I may not take quite as much care

I take just as much care as ever

7. I can laugh and see the funny side of things

As much as I always could

Not quite so much now

Definitely not so much now

Not at all

8. I feel restless as if I have to be on the move

Very much indeed

Quite a lot

Not very much

Not at all

9. Worrying thoughts go through my mind

A great deal of the time

A lot of the time

Not too often

Very little

10. I look forward with enjoyment to things

As much as I ever did

Rather less than I used to

Definitely less than I used to

Hardly at all

11. I feel cheerful

Never

Not often

Sometimes

Most of the time

12. I get sudden feelings of panic

Very often indeed

Quite often

Not very often

Not at all

13. I can sit at ease and feel relaxed

Definitely

Usually

Not Often

Not at all

14. I can enjoy a good book or radio or television programme

Often

Sometimes

Not Often

Very Seldom

DERMATOLOGY LIFE QUALITY INDEX

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please mark the correct answer with an 'X' on the corresponding line.

1. Over the last week, how **itchy, sore, painful** or **stinging** has your skin been?

Very much	1_____
A lot	2_____
A little	3_____
Not at all	4_____

2. Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?

Very much	1_____
A lot	2_____
A little	3_____
Not at all	4_____

3. Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?

Very much	1_____
A lot	2_____
A little	3_____
Not at all	4_____
Not relevant	5_____

4. Over the last week, how much has your skin influenced the **clothes** you wear?

Very much	1_____
A lot	2_____
A little	3_____
Not at all	4_____
Not relevant	5_____

5. Over the last week, how much has your skin affected any **social** or **leisure** activities?

Very much	1_____
A lot	2_____
A little	3_____
Not at all	4_____
Not relevant	5_____

6. Over the last week, how much has your skin made it difficult for you to do any **sport**?

Very much	1_____
A lot	2_____
A little	3_____
Not at all	4_____
Not relevant	5_____

7. Over the last week, has your skin prevented you from **working** or **studying**?

Yes	1_____
No	2_____
Not relevant	3_____

If "No", over the last week how much has your skin been a problem at **work** or **studying**?

A lot	1_____
A little	2_____
Not at all	3_____

8. Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?

Very much	1_____
A lot	2_____
A little	3_____
Not at all	4_____
Not relevant	5_____

9. Over the last week, how much has your skin caused any **sexual difficulties**?

Very much	1_____
A lot	2_____
A little	3_____
Not at all	4_____
Not relevant	5_____

10. Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?

Very much	1_____
A lot	2_____
A little	3_____
Not at all	4_____
Not relevant	5_____

Appendix B

Interviewer-Administered Instrument Developed by Yosipovitch *et al*

Questionnaire for Pruritus Assessment

Date : _____

Personal Information

Subject No: _____

Sex : Male Female

Age : Family Status : S M D W

Years of Education : _____

Ethnicity :_____

Handedness : R L B

Profession : _____

Currently Working : Yes / No

Medical Background

Diagnosis (es): _____

_____

Medications: _____

_____

1. Pruritus History

Subject currently suffers from pruritus Yes No

Subject suffered from pruritus in the past (more than ½ year ago) Yes No

When _____

Pruritus Duration (current or previous) _____

Pruritus Frequency

1. Almost every day
2. Every week
3. Every month
4. Seldom

Circumstances of pruritus onset: _____

Circumstances surrounding the end of pruritus (if applicable): _____

_____

Symptoms accompanying pruritus :

1. Pain in the pruritic area
2. Sweating
3. Headache
4. Heat sensation
5. Cold sensation
6. Other _____

CURRENT TREATMENT OF PRURITUS

Systemic	Local	Physical	Other
1. antihistamine	1. emoliants	1. TENS	
2. tricyclics	2. menthol	2. UVB	
3. serotonin antagonist	3. counterirritants	3. PUVA	
4. morphine antagonist	4. antihistamine		
5. cholestyramine	5.topical anesthetic		
6. aspirin	6. crotamiton		
	7. steroids		
	8. capsaicin		
	9. doxepin		

Effect of current treatment :

1. No effect
2. Short term effect (less than 24hrs)
3 Long term effect (more than 24 hours)

In your opinion, why do you suffer from pruritus? _____

_____

2. Pruritus Characteristics

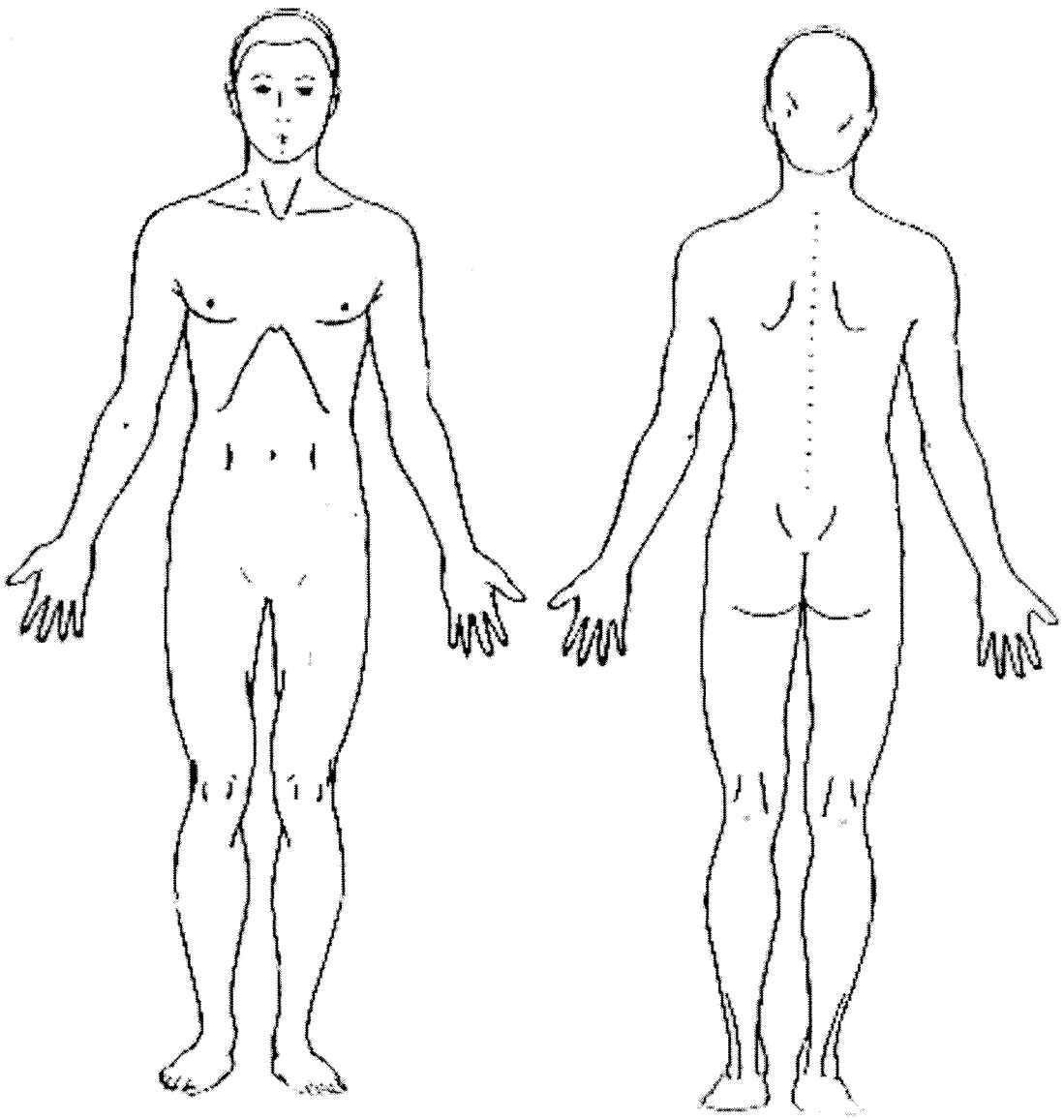
A. Location

Which areas of the subject's body are involved: _____

_____

Percent of subject's body surface area involved: _____

Is the pruritus symmetrical : Yes No



***B. CHARACTER OF SENSATION**

To which extent does the following descriptions match your pruritus:

	not at all	to a small extent	to a moderate extent	to a great extent
Tickling				
Stinging				
Crawling (like ants)				
Stabbing				
Pinching				
Burning				
Bothersome				
Annoying				
Unbearable				
Worrisome				

***3. THE DAILY CHANGES OF THE PRURITUS**

For each part of the day please indicate :

1. What is the frequency of appearance

a) Not itching
b) Occasional
c) Often
d) Always present

2. What is the time- pattern

a) Continuous
b) Episodic
c) Momentary

Time	**Frequency**	**Time pattern**
Morning		
Noon		
Evening		
Night		

Pruritus and sleep

Please indicate how often does any of the following happen :

1. Almost always
2. Sometimes
3. Never

Difficulty falling asleep	
Awakening by pruritus	
Use of sleeping medications	

Influences on pruritus

Please indicate how any item affects your pruritus :

1. Increases
2. Does not affect
3. Relieves

Sleep		Hot Water	
Rest		Cold Water	
Activity		Dryness	
Lying		Sweat	
Sitting		Cold	
Stress		Heat	
Fatigue			
Eating			
Physical Effort			
Specific Fabrics			

4. Intensity of Pruritus

Please indicate below the intensity of the pruritus as follows:

1. No Itching
2. Weak
3. Moderate
4. Strong
5. Very Strong

State of Pruritus	Intensity	VAS
Now		
In its worst state		
In its best state		
Itch after a mosquito bite		

Visual Analogue Scale

Please mark on the lines below the intensity of itching that you experience in the following states :

1. Now

None _____ Very strong

2. Pruritis in its worst state

None _____ Very strong

3. Pruritus in its best state

None _____ Very strong

4. Itch after a mosquito bite

None _____ Very strong

5. Coping with the pruritus

Has your mood changed because of the pruritus

1. No Change
2. Depressed
3. More Agitated
4. Difficulty in concentration
5. Anxious
6. Other

Have your eating habits changed because of the pruritus Yes No

Did you start a special diet because of the pruritus Yes No

Sexual Desire

1. No Change
2. Decreased
3. Non Existent

Sexual Function

1. No Change
2. Decreased
3. Non Existent

Did you find a way to relieve the pruritus: Yes No

How? _____

With what do you scratch (e.g, hand, legs, brush, etc.): _____

_____

Appendix C

The Itch Severity Scale

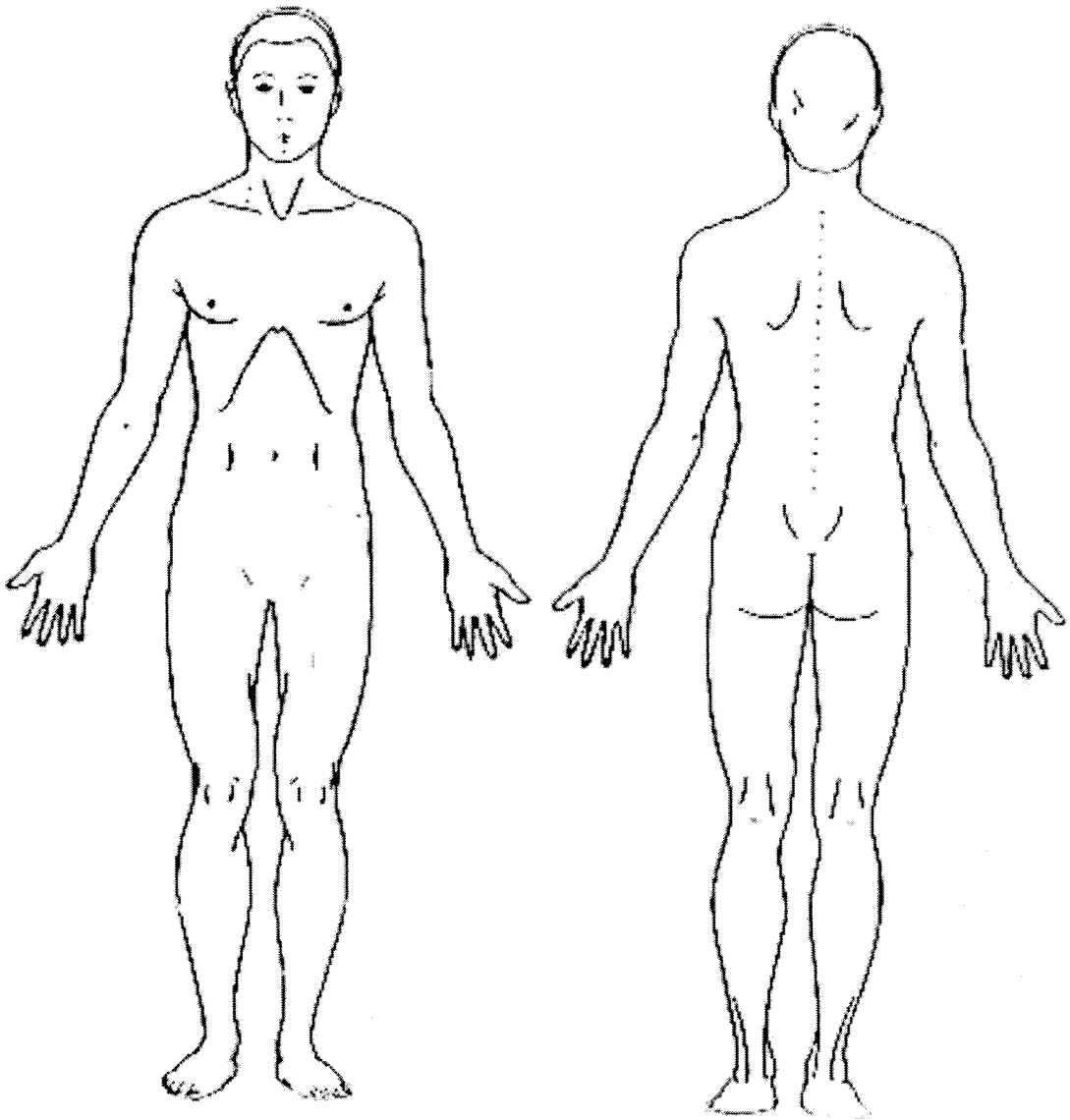
1. For each part of the day, what is the frequency of appearance of the itch (please put an 'X' in the box that corresponds with your answer)?

	Never itchy	Occasionally itchy	Often itchy	Always itchy
Morning				
Noon				
Evening				
Night				

2. To what extent do the each of the following describe the itch (please put an 'X' in the box that corresponds with your answer):

	not at all	to a small extent	to a moderate extent	to a great extent
Stinging				
Stabbing				
Burning				
Annoying				
Unbearable				
Worrisome				

3. Please shade in the areas where you tend to be itchy.



4. Please indicate the intensity of itch for each of the following (please put an 'X' in the box that corresponds with your answer):

	None	Weak	Moderate	Strong	Very strong
Itch in its average state					
Itch in its worst state					
Itch in its best state					

5. Has your mood changed because of the itch (you may circle more than one answer)?

a. No change
b. Depressed
c. More agitated
d. Difficulty in concentration
e. Anxious

6. How has itch affected the following (please put an 'X' in the box that corresponds to your answer):

	No change	Decrease
Sexual desire		
Sexual function		

7. Please indicate how often any of the following happens (please put an 'X' in the box that corresponds with your answer):

	Never	Sometimes	Almost always
Difficulty falling asleep due to itch			
Awakening due to itch			
Use of sleep medications			