ASSOCIATIONS AMONG DISEASE SEVERITY, PHYSICAL ACTIVITY, AND QUALITY OF LIFE IN PSORIASIS

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Abstract

Psoriasis is the most common auto-immune disorder worldwide and most often manifests itself as scaly plaques on the skin. It can substantially affect a person's quality of life (QOL) and overall wellness. In addition, individuals with moderate-to-severe psoriasis are likely at greater risk for chronic co-morbidities like cardiovascular disease, type 2 diabetes, obesity, and metabolic syndrome. There is currently a dearth of literature evaluating the lifestyle habits of individuals with psoriasis, especially in regards to physical activity (PA). This exploratory, cross-sectional study examined the PA habits of people with psoriasis and explored whether PA was related to psoriasis severity and QOL. The results suggest that total PA was not related to psoriasis severity. However, individuals with more severe disease were less physically active in their leisure time. In addition, symptoms such as itchiness, stinging, soreness, and pain showed a strong inverse association with leisure PA, independent of the body surface area involved. Physical and psychological aspects of QOL were not strongly related to leisure PA. Overall, it appears that individuals with more severe disease, as measured by a combination of symptoms, are less physically active in their leisure time, which could contribute to some of the co-morbidities seen in moderate-to-severe psoriasis.

Table of Contents

List of Tables

List of Figures

Abbreviations

BMI	body mass index
BSA	body surface area
CAD	coronary artery disease
CBT	cognitive-behavioral therapy
CI	confidence interval
CVD	cardiovascular disease
DLQI	Dermatology Life Quality Index
g	grams
IL	interleukin
IPAQ	International Physical Activity Questionnaire
lbs	pounds
LDL-C	low-density lipoprotein cholesterol
LPHES	Laboratory of Physiological Hygiene and Exercise Science
MET	metabolic equivalent
OR	odds ratio
oz	ounces
PA	physical activity
PASI	Psoriasis Area and Severity Index
PsA	psoriatic arthritis
QOL	quality of life
RR	relative risk
SAPASI	Self-Administered Psoriasis Area and Severity Index
SD	standard deviation
T2D	type II diabetes
Th1	T-helper 1
Th17	T-helper 17
TNF-α	tumor necrosis factor-alpha
WHOQOL	World Health Organization Quality of Life

Chapter 1: Introduction

Psoriasis is a chronic, incurable skin disease that significantly impacts quality of life (QOL) (Krueger et al., 2001; Rapp, Feldman, Exum, Fleischer Jr, & Reboussin, 1999). Several variants of psoriasis exist, with the most common type being psoriasis vulgaris, accounting for approximately 90% of cases (Griffiths & Barker, 2007). Psoriasis is typically characterized by raised areas of erythematous skin, which are often covered by silvery white scaling (Langley, Krueger, & Griffiths, 2005). Sites typically affected include the elbows, knees, and scalp, while more sensitive or visual areas such as the genitals, hands, nails, and face can be involved (Ramsay & O'Reagan, 1988). Psoriasis can cause physical pain, sensitivity, pruritus (itching), burning, and bleeding (Sampogna et al., 2004). Symptoms are often cyclical with periods of flare-ups and remissions (Krueger & Duvic, 1994). Although estimates vary based on population demographics and study designs employed, approximately 2-3% of Americans suffer from psoriasis (Koo, 1996; Stern, Nijsten, Feldman, Margolis, & Rolstad, 2004).

The thick, red lesions of the skin—and the accompanying psychological effects—have long-been the primary focus of concern for researchers and practitioners treating psoriasis. More recently, however, it has become increasingly evident that those with psoriasis may be at greater risk for a host of chronic diseases, as associations between psoriasis and cardiovascular disease (CVD) (Friedewald et al. 2008; Gelfand et al., 2006; Tobin et al., 2010), type II diabetes (T2D) (Cohen et al., 2008; Shapiro et al., 2007), obesity (Herron et al., 2005; Neimann et al., 2006; Setty, Curhan, & Choi, 2007), and metabolic syndrome (Gisondi & Girolomoni, 2010; Love et al., 2011) are now established. Importantly, the risk of developing these so-called cardiometabolic co-morbidities appears to be positively related to psoriasis disease severity (Azfar & Gelfand, 2008).

Physical activity (PA) is now well-accepted as a vital component for the prevention and treatment of the CVD, T2D, obesity, and metabolic syndrome (Churilla & Zoeller, 2008; Fogelholm, Stallknecht, & Van Baak, 2006; Gaesser, 2007; Jolliffe et al., 2001; Knowler et al., 2002; Thomas, Elliott, & Naughton, 2006). Despite grounds to suspect that PA could help attenuate or prevent some of the cardiometabolic co-morbidities associated with psoriasis, it is surprising to note that practically no research has been completed in this area. Furthermore, although there is evidence to demonstrate that PA dose-dependently improves QOL in healthy

individuals (Martin, Church, Thompson, Earnest, & Blair, 2009), the association between PA and QOL in psoriasis patients is unknown. To date, only a handful of published studies have examined the PA patterns of people with psoriasis (Herron et al., 2005; Kavli, Forde, Arnesen, & Stenvold, 1985; Mallbris, Granath, Hamsten, & Ståhle, 2006; Prizment et al., 2011; Qureshi, Dominguez, Choi, Han, & Curhan, 2010). Importantly, these studies did not distinguish whether PA varied by psoriasis severity, and hence, whether low levels of PA could potentially account for some of the increased risk of cardiometabolic co-morbidities and reduction in QOL seen in patients with moderate-to-severe psoriasis. In addition, PA was not a specific interest for any of these investigations.

The study of PA in association with psoriasis severity and QOL is relevant for several reasons. Data on these parameters could help determine whether specific individuals with psoriasis are targets for PA interventions. Preliminary evidence supporting the notion that lifestyle modifications such as PA could alter psoriasis disease course, reduce cardiometabolic co-morbidities, and improve QOL could provide justification for more research into an area that is vastly understudied. As psoriasis is a lifelong disease, understanding the influence of lifestyle behaviors on the disease course and management of psoriasis is imperative.

Based on the current state of the literature, the purpose of this investigation is to perform an exploratory, cross-sectional study of the associations between disease severity, PA, and QOL in individuals with psoriasis. In addition, the study aims to answer the following specific questions:

1) Is psoriasis severity negatively associated with PA?
2) Which specific signs and symptoms of psoriasis, if any, are most strongly associated with PA?
3) Is PA positively associated with QOL in psoriasis, and if so, what aspects of QOL show the strongest associations?

Chapter 2: Literature Review

Introduction

In order to understand the potential associations between psoriasis severity, PA, and QOL, a basic review of psoriasis is necessary. The following passages will discuss several important features of psoriasis, including the epidemiology, pathophysiology, disease burden, and cardiometabolic co-morbidities of psoriasis. With this framework in mind, the discussion will move to review past literature that has examined PA and psoriasis in some way or another. Finally, literature that supports the proposed research questions will be reviewed.

Psoriasis Epidemiology

Although estimates vary based on population demographics and study designs employed, approximately 2-3% of Americans suffer from psoriasis (Koo, 1996; Stern et al., 2004). Studies from around the world estimate psoriasis prevalence to range anywhere from 0.6 to 4.8% (Neimann, Porter, & Gelfand, 2006). Sex does not generally influence the development of psoriasis, as both men and women are equally affected (Nevitt & Hutchinson, 1996). Psoriasis risk varies with racial background, and white populations are typically afflicted more frequently than other racial groups (Neimann, Porter, & Gelfand, 2006). Geographic region influences psoriasis prevalence, with warmer regions in both the northern and southern hemispheres demonstrating the lowest prevalence (Braathen, Botten, & Bjerkedal, 1989; Duffy, Spelman, & Martin, 1993).

Most cases of psoriasis are considered mild based on the percentage of body surface area (BSA) involved. In most studies, approximately two-thirds of cases are considered mild, which is usually defined by less than 1-2% of BSA involvement (about the size of 1-2 hand palms). Twenty-five percent of cases are moderate (3-10% BSA) and 10% are severe (>10% BSA) (Koo, 1996; Stern et al., 2004). Despite most cases being defined as mild based on BSA, location of psoriatic lesions can substantially modify patient-perceived disease severity. Lesions on the face, hands, and nails can carry substantial burdens even when the absolute BSA covered may be small (de Jong, Seegers, Gulinck, Boezeman, & van de Kekhof, 1996; Fortune, Main, O'Sullivan, & Griffiths, 1997b; Pettey, Balkrishnan, Rapp, Fleischer, & Feldman, 2003). In

addition, symptoms such as pain, itching, and flaking may be more predictive of QOL than overall percentage of BSA coverage (de Korte, Sprangers, Mombers, & Bos, 2004).

Psoriasis can appear at any time in life, and the average age of diagnosis has been estimated to be 33 years (Nevitt & Hutchinson, 1996). Some research suggests that psoriasis incidence is bimodally distributed, with peaks in the 20s and 50s (Ferrándiz, Pujol, García-Patos, Bordas, & Smandía, 2002; Smith, Kassab, Rowland Payne, & Beer, 1993). In addition, age of onset appears to be associated with different clinical characteristics of the disease. The late onset variety appears to be more sporadic with less genetic hereditability, potentially being influenced more by lifestyle and environmental factors (Ferrándiz et al., 2002; Henseler & Christophers, 1985).

Pathophysiology of Psoriasis

Psoriasis arises from abnormalities in epidermal skin cell proliferation and differentiation (Weinstein, McCullough, & Ross, 1985). Keratinocytes of the skin—stratified, squamous, epithelial cells—do not reach terminal differentiation, which is required to form the granular layer of the epidermis. Instead, the incompletely differentiated keratinocytes layer to form a thickened stratum corneum, prominent with hyperproliferative keratinocytes that retain their nuclei—known as parakeratosis (Krueger & Bowcock, 2005). Additionally, angiogenesis and blood vessel dilatation in the dermal layer are prominent in psoriasis, contributing to symptoms of redness and swelling (Hern, Stanton, Mellor, Levick, & Mortimer, 1999). Laser Doppler blood flow measurement has shown cutaneous blood flow at psoriasis plaques to be 9-13 times higher than at normal skin sites (Hern et al., 1999). Several cellular proteins and inflammatory cytokines appear to elicit these changes, including an increased production of vascular endothelial growth factor and vascular permeability factor. These factors are released early in psoriatic lesion development and are pivotal in supplying the nutritional and cellular inflammatory factors necessary for lesion development and maintenance (Krueger & Ellis, 2005).

Psoriasis can in part be explicated via immune-mediated aberrations. Infiltration by several types of immune cells into the dermal and epidermal layers is a hallmark feature of psoriasis, making a clear delineation of psoriasis immunopathology complicated. Several comprehensive reviews outline the role of the immune system in the pathogenesis of psoriasis

(Griffiths & Barker, 2007; Guttman-Yassky & Krueger, 2007; Liu, Krueger, & Bowcock, 2007). Neutrophils can often be found spread diffusely throughout the parakeratosis dominated stratum corneum (Murphy, Kerr, & Grant-Kels, 2007). The dermis is predominantly infiltrated by clusters of T-cells and dendritic cells (Lowes, Bowcock & Krueger, 2007). Research exists to suggest that these T-cells and dendritic cells located in the dermis are pivotal in the pathogenesis of psoriasis (Krueger & Ellis, 2005). Dendritic cells, or other antigen presenting cells, migrate from the skin to local lymph nodes, at which point they present an antigen to naïve T-cells. Antigen presentation causes naïve T-cells to become activated and produce memory T-cells, at which point the memory T-cells travel back to the skin where they can be re-activated (Krueger & Ellis, 2005). The activated T-cells contribute to the release of numerous cytokines, including tumor necrosis factor-alpha (TNF-α), causing the cell-mediated immune responses responsible for the histological and clinical signs seen in psoriasis (Lowes, Bowcock, & Krueger, 2007).

Psoriasis previously was thought to be mediated primarily via the T-helper 1 (Th1) cell and its associated cytokines (Blauvelt, 2008). Recently, however, the identification of a unique T-cell—T-helper 17 (Th17)—has challenged this view, as these Th17 cells have since been found abundantly in psoriatic plaques (Lowes et al., 2008). Th17 cells are responsible for the production of cytokines interleukin (IL)-17A and IL-22, which are at least partially responsible for the hyperproliferation of keratinocytes (Fitch, Harper, Skorcheva, Kurtz, & Blauvelt, 2007). Another cytokine, IL-23, is excessively produced by DC and keratinocytes in psoriasis. IL-23 regulates the survival and proliferation of Th17 cells, thus serving as a pivotal player in the immune-mediated milieu of psoriasis (Blauvelt, 2008).

While T-helper cells such as Th1 and Th17 are over-expressed in psoriasis, regulatory or suppressor T-cells seem to be reduced and may contribute to the inability of the immune response to ‘shut off’ (Sugiyama et al., 2005). Indeed, this type of imbalance between immune response and immune suppression has been documented in other autoimmune diseases, such as multiple sclerosis (Viglietta, Baecher-Allan, Weiner, & Hafler, 2004).

Genetic factors play a prominent role in the development of psoriasis. Up to nearly 10% of the population carries the genotype for psoriasis (Swanbeck, Inerot, Martinsson, & Wahlström, 1994), and the heritability has been estimated to be between 60-90% (Elder et al., 1994). Siblings of an individual with psoriasis have a 4-6 relative risk (RR) of developing psoriasis compared to a non-relative (Roberson & Bowcock, 2010), and twin studies demonstrate

that monozygotic twins have psoriasis concordantly more frequently than dizygotic twins (67% vs. 18%) (Krueger & Ellis, 2005). Genetic scans for psoriasis susceptibility loci have identified many potential linkages, but only the major histocompatibility complex locus on chromosome 6p21 has consistently been linked to psoriasis (Liu, Krueger, & Bowcock, 2007).

Environmental factors also play a role in the development and exacerbation of psoriasis, although there is a general dearth of knowledge in this area. Smoking (Naldi et al., 2005), alcohol use (Behnam, Behnam, & Koo, 2005), infections (Mallon et al., 1998), emotional stress (Naldi et al., 2005), and certain medications (Tsankov, Angelova, & Kazandjieva, 2000) have all been identified as potential disease aggravators. Increased attention to the role of obesity in the development of psoriasis was recently highlighted by a large, prospective cohort study. As a part of the Nurses' Health Study II, 78,626 women were followed prospectively for 14 years to determine the associations between various adiposity measures and the incidence of psoriasis (Setty, Curhan, & Choi, 2007). Graded positive associations were found between waist circumference, hip circumference, waist-to-hip ratio, body mass index (BMI), and the incidence of psoriasis. Most interestingly, weight gain from 18 years of age was associated with an increased risk of psoriasis. Compared to women who had maintained their weight [-5.0 to +4.9 pounds (lbs)], women who had gained 30-34.9 and >35 lbs between age 18 and weight updated every 2 years had a RR of psoriasis of 1.35 [95% confidence interval (CI), 1.01-1.80] and 1.88 (95% CI, 1.44-2.46), respectively. These data suggest that obesity and weight gain are moderate risk factors for psoriasis, and based on the high prevalence of obesity in the United States, the prevention of weight gain could have a substantial impact on the public health burden of psoriasis.

Burden of Psoriasis

Because of its re-occurring, unpredictable, and visible nature, psoriasis can carry substantial psychological, social, and physical burdens. Such was the case in a survey of National Psoriasis Foundation members, which demonstrated that dissatisfaction with treatments, fear of disease progression, depression, and embarrassment were common issues among respondents (Krueger et al., 2001). Kurd, Troxel, Crits-Christoph, and Gelfand (2010) examined the associations between psoriasis and clinical diagnoses of depression, anxiety, and suicidality. Patients with psoriasis had higher hazard ratios for depression (1.39; 95% CI, 1.37-1.41), anxiety

(1.31; 95% CI, 1.29-1.34), and suicidality (1.44; 95% CI, 1.32-1.57) when compared to controls. Compared to those with mild psoriasis, subjects with severe psoriasis were more likely to be diagnosed with depression and suicidality, but not anxiety (Kurd et al., 2010). Additional studies have also noted that patients with psoriasis may experience suicidal thoughts at greater frequency, with up to 10% reporting suicide ideation or a wish to be dead (Gupta, Schork, Gupta, Kirkby, & Ellis, 1993; Picardi, Mazzotti, & Pasquini, 2006).

Psoriasis has been shown repeatedly to impact QOL in a number of populations (de Korte et al., 2004; Krueger et al., 2001; Rapp et al., 1999). When compared to other chronic diseases, it is evident that psoriasis can significantly decrease QOL. Rapp et al. (1999) compared scores from a QOL questionnaire from psoriasis patients to patients with 10 other common chronic diseases known to significantly impact QOL. Based on this patient-centered assessment, patients with psoriasis ranked 10^{th} and 9^{th} in physical and mental functioning, respectively. Only individuals with congestive heart failure had lower physical functioning scores, while only individuals with depression and chronic lung disease had lower mental functioning scores (Rapp et al., 1999).

Many individuals with psoriasis also suffer from psoriatic arthritis (PsA), an inflammatory arthritis that affects approximately 10-30% of people with psoriasis (Gelfand et al., 2005; Zachariae, 2003). Symptoms can include pain, swelling, and tenderness of joints in an asymmetrical manner. Other features that distinguish PsA from other inflammatory joint diseases include distal interphalangeal joint involvement, dactylitis, enthesitis, and negative rheumatoid factor (Gladman, Antoni, Mease, Clegg, & Nash, 2005). Degenerative joint disorders decrease physical functioning and increase disability in a large number of patients. PsA results in comparable disability and reductions in QOL when compared to other joint disorders such as rheumatoid arthritis (Husted, Gladman, Farewell, & Cook, 2001; Sokoll & Helliwell, 2001).

The impairment in QOL psoriasis patients experience can translate into a loss of productivity. In a study of 201 psoriasis patients, QOL was significantly predictive of loss of work productivity, while objective clinical disease severity was not (Schmitt & Ford, 2006). Moreover, a study of 369 psoriasis patients from the United Kingdom found 59% of working patients with severe psoriasis had lost a mean of 26 days from work during the previous year (Finlay & Coles, 1994). Of the 369 patients, 180 were not working, and 34% of them attributed this to their psoriasis.

Although there have been immense progress in psoriasis treatments over the past several decades, many of them are expensive. Patel et al. (as cited in Strober, 2008) reported annual out-of-pocket expenses for patients range from $1,600-2,200 and do not change significantly with psoriasis severity. Biologics, which will continue to gain more widespread use for moderate-to-severe psoriasis because of their high efficacy rates, typically cost more than $20,000 per year without insurance coverage (Beyer & Wolverton, 2010). Unfortunately, patients with severe psoriasis are more likely to earn and work less than patients with mild psoriasis (Horn, Fox, Patel, Chiou, Dann, & Lebwohl, 2007b), potentially limiting access to medications for the patients that need them most.

Discordance often exists between practitioners and patients regarding the severity of a patient's psoriasis. As outlined by the National Psoriasis Foundation Clinical Consensus on Disease Severity, patients frequently believe that those around them—even their attending physicians—under-appreciate the severity of their condition (Pariser et al., 2007). Changes in treatment recommendations now recognize that systemic therapy and/or phototherapy—usually reserved for extensive skin involvement—should be considered for patients even with minimal BSA involvement if it causes significantly disability (Pariser et al., 2007). In light of these findings, it would be ill-advised for practitioners to solely evaluate psoriasis severity based on BSA involvement; it would be prudent to take a more holistic approach to evaluation (e.g. QOL measures, physical pain, etc.), since objective disease severity does not always reflect the patient's overall QOL.

Psoriasis Cardiometabolic Co-Morbidities

Psoriasis and cardiovascular disease.

Emerging evidence indicates that psoriasis and CVD share common pathological pathways. Activation of T-cells within lymph nodes, migration and adhesion of T-cells to the blood vessel endothelium, passage of T-cells across the endothelial barrier via adhesion molecules, subsequent T-cell interaction with various cellular components, and the secretion of cytokines are all shared steps in both atherosclerotic and psoriatic plaque development (Ghazizadeh et al., 2010).

In 1978, McDonald and Calabresi recognized a two-fold increase in the incidence of vascular disease in patients with psoriasis. Since that time, many studies have attempted to

establish a link between psoriasis and various cardiovascular diseases. One of the largest studies on CVD and psoriasis comes from a cohort of 130,976 patients in Great Britain (Gelfand et al., 2006). With an average follow-up of 5.4 years, the authors found evidence to indicate that the rate of acute myocardial infarction (AMI) was higher in patients with psoriasis than in controls. After adjusting for other risk factors, a 30-year-old patient with mild or severe psoriasis had significantly higher AMI RRs of 1.29 (95% CI, 1.14-1.46) and 3.10 (95% CI, 1.98-4.86), respectively. The RR of AMI was actually attenuated with age, with a 60-year-old patient with mild or severe psoriasis having RRs for AMI of 1.08 (95% CI, 1.03-1.13) and 1.36 (95% CI, 1.13-1.64).

Furthermore, coronary heart disease (CAD) is the leading cause of death in patients with psoriasis, and compared to the general population, patients with psoriasis present with elevated levels of many of the risk factors known to contribute to CAD (Friedewald et al. 2008). For example, Gelfand et al. (2006) demonstrated hypertension prevalence rates of 20%, 15%, and 12% in severe psoriasis, mild psoriasis, and controls. The prevalence of hyperlipidemia was also increased in psoriasis: 6%, 5%, and 3% of patients with severe psoriasis, mild psoriasis, and no psoriasis were hyperlipidemic. Low-density lipoprotein cholesterol (LDL-C) and high-density lipoprotein cholesterol tend to show atherogenic patterns in psoriasis patients, with disease severity often correlating with the degree of dyslipidemia (Reynoso-von Dratel, Martínez-Abundis, Balcázar-Muñoz, Bustos-Saldaña, & González-Ortiz, 2003; Rocha-Pereira, Santos-Silva, Rebelo, Figueiredo, & Quintanilha, 2001).

An extensive literature review by Tobin et al. (2010) used 14 studies published between 1975 and 2009 to evaluate the association between psoriasis and CVD. They concluded that substantial evidence indicates an increased risk of developing CVD in patients with psoriasis, with the strongest evidence in patients with more severe disease and longer disease duration.

There is not universal agreement, however, that patients with psoriasis are truly at increased risk for CVD. As discussed by Nijsten and Wakkee (2009), psoriasis patients are more likely to visit their physician, which may ultimately engender more frequent diagnosis of CVD or its risk factors than in the general "healthy" population. Other factors that may confound the issue include increased usage of medications that can contribute to CVD (cyclosporine or topical steroids) and residual confounding from other lifestyle factors such as smoking and excessive alcohol use. And even in those patients that may be at increased risk for CVD, the use of

psoriasis as an independent risk factor to help guide treatment decisions may not be particularly useful (Stern, 2010).

Future research will likely aim to determine which risk factors are most predictive of CVD in psoriasis populations and whether the modest increase in CVD risk is primarily due to the inflammatory nature of psoriasis, poor lifestyle choices of psoriasis patients, or both. Importantly, the effect of different treatment regimens (both pharmacological and lifestyle) on CVD morbidity and mortality in psoriasis needs to be clarified.

Psoriasis, type II diabetes, and insulin resistance.

Several reports have found an association between psoriasis and T2D and/or insulin resistance. A cross-sectional study from Cohen et al. (2008) studied 16,851 patients with psoriasis in order to determine whether the prevalence of T2D was higher than in controls. After adjusting for age and gender, psoriasis was significantly associated with T2D (odds ratio (OR), 1.58; 95% CI, 1.49-1.68). In a subset of 9,228 patients, psoriasis was still associated with T2D after an additional adjustment for obesity (OR, 1.23; 95% CI, 1.10-1.37).

These findings are similar to and in line with several other reports, which have found ORs and prevalence of similar magnitude (Henseler & Christophers, 1995; Neimann et al., 2006; Shapiro et al., 2007). Much like CVD, it is difficult to determine causality from the available evidence because of the inherent complicatedness of separating the effect of psoriasis from other negative lifestyle behaviors commonly found in these individuals.

Psoriasis and obesity.

The rate of obesity in the United States has been increasing at an alarming rate over the past 30 years (Ogden & Carroll, 2010). Although significant debate persists, the rise in obesity is likely attributable to a decrease in PA and an increase in the availability of calories in the food supply, especially from foods that are calorically dense and nutrient-poor (Wyatt, Winters, & Dubbert, 2006).

In a study of psoriasis patients in the United Kingdom, Neimann et al. (2006) found that patients with mild and severe psoriasis had significantly higher adjusted ORs of obesity (1.27; 95% CI 1.24-1.31, and 1.79; 95% CI 1.55-2.05, respectively) compared to controls. Likewise, rates of obesity were nearly twice that of controls (35% vs. 18%) in the Utah Psoriasis Initiative

study (Herron et al., 2005). Cross-sectional data, however, cannot differentiate whether psoriasis preceded obesity or whether obesity preceded psoriasis. The Nurses' Health Study II data discussed previously provides some support that obesity may precede the development of psoriasis in a number of cases (Setty, Curhan, & Choi, 2007).

Physical Activity and Psoriasis

Physical activity patterns in psoriasis.

Surprisingly, little research has directly examined the PA patterns of individuals with psoriasis, with only a few studies reporting PA patterns in some psoriasis populations (Herron et al., 2005; Kavli et al., 1985; Mallbris et al., 2006; Prizment et al., 2011; Qureshi et al, 2010). In a cross-sectional study on the associations between smoking, obesity, and psoriasis management, Herron et al. (2005) found that obese psoriasis subjects were less physically active than non-obese psoriasis subjects, with 43% of the obese subjects compared to 59% of non-obese subjects engaging in PA in the previous month. PA was defined as 2-3 times per week at a minimum of 30 minutes per session. Details of how this information was collected were not provided, and the results were not compared to a healthy population. In addition, it is not surprising that obese individuals would report engaging in less PA than non-obese individuals, regardless of whether they have psoriasis or not.

In a survey of 14,667 adult men and women, Kavli et al. (1985) asked about the frequency of PA at work and during leisure time, as well as whether the subjects had ever been diagnosed with psoriasis. PA was rated on a 1-4 scale. Respondents were divided into four PA patterns for both work and leisure: sedentary, moderate, intermediate, or heavy. Using a multiple regression model with seven other variables (smoking status, smoking amount, coffee consumption, fruit/vegetable intake, psoriasis family history, joint pain, rheumatoid arthritis diagnosis), PA at work in women showed a significant negative association with psoriasis prevalence ($p < 0.05$). In men, PA at work showed a trend towards a negative association with psoriasis prevalence, but the association was not significant. PA during leisure time was not significantly associated with psoriasis prevalence in men or women.

Mallbris et al. (2006) compared blood lipids of individuals with a diagnosis of psoriasis within the preceding 12 months to healthy controls. PA leading to perspiration or an increase in body temperature lasting at least 30 minutes was the threshold used. An ordinal 5-point scale was

used to define the number of exposures per week or month. Psoriasis cases had similar PA patterns compared to matched controls, with 33% of psoriasis cases reporting no regular PA compared to 30% of controls. Approximately 50% cases and 56% of controls reported engaging in PA more than once per week.

A recent analysis of the Nurses' Health Study II indicated that low PA could be a potential risk factor for the development of psoriasis (Qureshi et al, 2010). The main objective of the study was to determine whether beer consumption was a risk factor for developing psoriasis. The authors adjusted for PA in a multivariate analysis because it appeared to be a confounder. Specific statistics on how psoriasis incidence varied by different levels of PA were not reported. The details of the self-administered questionnaire used to collect the PA data have been reported elsewhere (Wolf et al., 1994).

The most recent study relating psoriasis and PA comes from an analysis of the Iowa Women's Health Study data. Prizment et al. (2011) aimed to determine whether psoriasis in women over age 65 was associated with the incidence of cancer. Diagnosis of psoriasis was determined from Medicare claims records. In the analysis, the investigators also examined what baseline characteristics, including PA, were associated with psoriasis. Of the women without psoriasis, 42.1% reported engaging in regular PA, as compared to 36.3% of women with a diagnosis of psoriasis. After adjusting for age, women who engaged in regular PA had 0.8 odds of psoriasis (95% CI, 0.7-0.9) as compared to women not engaging in regular PA. The odds remained similar (0.8; 95% CI 0.7-1.0) after adjusting for additional variables (education, smoking status, pack-years of smoking, alcohol, and BMI). The study is somewhat limited, however, because only PA data collected at baseline in 1986 was used in the analysis while the psoriasis diagnosis claims were ascertained from 1991-2004. Therefore, limited conclusions can be drawn in regards to how PA actually related to psoriasis diagnosis.

Overall, none of the main hypotheses from the above studies were directed towards PA, and none attempted to relate PA to disease severity. Furthermore, the majority of these studies relied on a few questions to assess PA instead of validated questionnaires or tools such as accelerometers. Despite this, the studies from Kavli et al. (1985), Qureshi et al. (2010), and Prizment et al. (2011) do provide some tenuous support that PA may be related to psoriasis prevalence and incidence. Based on these five studies, there is a clear gap in the research regarding the association between PA and psoriasis severity.

Potential mechanisms linking psoriasis severity, psoriasis cardiometabolic co-morbidities, and physical activity.

As research into the shared pathophysiological links between psoriasis and its cardiometabolic co-morbidities continues to grow, a better understanding of these disease clusters will emerge. Currently, however, there is significant evidence to suggest shared cellular and inflammatory pathways among these diseases and PA participation.

Excessive weight and adiposity.

Along with its energy-storing capabilities, fat tissue is now recognized as an active endocrine organ capable of secreting hormones and cytokines (Fantuzzi, 2005), some of which are implicated in the exacerbation of psoriasis. For example, TNF-α is elevated and a very effective target for therapy in psoriasis patients, but is also elevated in obese non-psoriasis patients (Hajer, Van Haeften, & Visseren, 2008). While human interventional studies directly assessing the effect of weight loss on psoriasis severity are lacking, complete remission of psoriasis after gastric bypass has been reported in individual cases (de Menezes Ettinger et al., 2006; Higa-Sansone et al., 2004). Additionally, a recent randomized, controlled trial comparing cyclosporine vs. cyclosporine plus weight loss in obese patients with moderate-to-severe psoriasis demonstrated a favorable effect of weight loss on treatment response (Gisondi et al., 2008). The method used to achieve weight loss was a calorie-restricted diet. After 24 weeks, 20/30 (66.7%) patients in the cyclosporine plus weight loss group (average weight loss of 7% of body weight) achieved a 75% reduction in their disease severity, compared to only 9/31 (29%) patients in the cyclosporine only group. Although exciting, caution is warranted because the reduced calorie diet could have contributed to the positive results by increasing intestinal cyclosporine absorption (Gelfand & Abuabara, 2010). Although the importance of PA in weight loss has long been debated, long-term maintenance of substantial weight loss is highly dependent on PA (Anderson, Konz, Frederich, & Wood, 2001; Tate, Jeffery, Sherwood, & Wing, 2007). Therefore, the influence of PA on weight loss and maintenance in psoriasis is an important subject for future research.

Inflammation.

As discussed, reductions in adiposity can reduce markers of inflammation. Interestingly, there is a growing body of evidence that supports some anti-inflammatory effects of PA beyond those derived from fat loss. For instance, mice that exercised 30 minutes daily had lower amounts of the pro-inflammatory cytokine TNF-α in skin wounds and experienced faster wound healing when compared to controls (Keylock et al., 2008). Human intervention studies also show that increasing PA through structured exercise can decrease circulating TNF-α, independent of fat loss. Sixteen overweight women exercising over a period of 12 weeks reduced their levels of TNF-α, using an exercise protocol of 30 minutes a day, 5 days a week at 70% maximum heart rate (StraÎczkowski et al., 2001). The changes in TNF-α occurred independently of changes in BMI, waist circumference, percentage body fat, plasma glucose, insulin, and free fatty acids. Another study of 27 overweight, Japanese women showed that as little as 30-45 minutes of moderate intensity aerobic exercise 4-5 days per week over five months was enough to reduce circulating levels of TNF-α (Tsukui et al., 2000). It remains unclear, however, whether these changes in circulating TNF-α from increasing PA could translate into any meaningful reductions in CVD incidence among patients with psoriasis. The ever-increasing use of TNF-α antagonist therapy (infliximab, entanercept, and adalimumab) for the treatment of various inflammatory driven diseases, including psoriasis (Melnikova, 2009), provides some circumstantial evidence that increasing PA could potentially help reduce CVD in psoriasis patients. In a presentation at the 2011 Annual Meeting of the American Academy of Dermatology, Wu (as cited in Lowry, 2011) presented data from a retrospective study of over 24,000 psoriasis patients showing that TNF-α antagonist therapy treated patients had an overall 48% reduced risk of experiencing an AMI.

Several other inflammatory cytokines share a link between psoriasis and its cardiometabolic co-morbdities. IL-6 contributes to the development of T2D (Kristiansen & Mandrup-Poulsen, 2005) and CAD (Danesh et al., 2008), and interferon-γ may be a regulator of atherosclerosis (McLaren & Ramji, 2009). Both interferon-γ (El Barnawi, Giasuddin, Ziu, & Singh, 2001; Szegedi et al., 2003) and IL-6 (Mizutani, Ohmoto, Mizutani, Murata, & Shimizu, 1997; Zalewska et al., 2006) are commonly elevated in psoriasis and often correlate strongly with disease severity. Evidence from non-psoriasis populations suggests that increasing PA could have a positive effect on reducing these inflammatory cytokines. In a population of 28 CAD

patients, levels of interferon-γ and IL-6 decreased significantly after 12 weeks of exercise training despite no changes in body weight (Goldhammer et al., 2005). Likewise, fasting IL-6 levels were reduced in a population of inactive, but otherwise healthy, middle-aged men after 12 weeks of moderate intensity aerobic exercise (Thompson et al., 2010). The reductions in IL-6 were maintained through 24 weeks of the exercise intervention, but after 2 weeks of detraining, IL-6 levels quickly returned to near baseline.

Oxidative stress.

Oxidative stress and excessive production of reactive oxygen species occur in psoriasis and can contribute to the development or worsening of the disease through several signal transduction pathways (Zhou, Mrowietz, & Rostami-Yazdi, 2009). In a group 35 psoriasis patients, activity levels of cellular anti-oxidant enzymes were blunted in comparison to control subjects while markers of oxidative stress were elevated (Vanizor Kural, Orem, Cimşit, Yandi, & Calapoglu, 2003). CAD, T2D, and metabolic syndrome are all characterized by increases in oxidative stress (Ceriello & Motz, 2004; Hansel et al., 2004).

Cross-sectional data support a negative association between PA and oxidative stress markers in some studies (Covas et al., 2002; Karolkiewicz et al., 2003) but not others (Kostka, Drai, Berthouze, Lacour, & Bonnefoy, 2000). Moderate levels of exercise up-regulate cellular anti-oxidant enzymes such as superoxide dismutase in interventional animal (Hollander et al., 2001) and human (Campbell et al., 2010; Elosua et al., 2003) studies, suggesting that PA could be helpful in reducing the oxidative stress load characteristic of psoriasis.

Serum lipids and lipid oxidation.

Serum lipids could potentially be involved simultaneously in the pathology of psoriasis and its cardiometabolic co-morbidities. Elevated levels of oxidized LDL-C have been found in psoriatic plaques, suggesting a possible role in the disease process (Tekin, Tekin, Barut, & Sipahi, 2007). Oxidized LDL-C is a sensitive marker of CAD (Holvoet et al., 2001) and is predictive of the development of metabolic syndrome in young adults (Holvoet, Lee, Steffes, Gross, & Jacobs, 2008). Increasing PA reduces total cholesterol, LDL-C, and oxidation of lipids in the blood (Vasankari, Kujala, Vasankari, & Ahotupa, 1998; Vuorimaa, Ahotupa, Irjala, & Vasankari, 2005; Wang, Lin, Chen, & Wong, 2000). Furthermore, a recent pilot study

demonstrating improvements in psoriasis severity with statin treatment lends support to this shared disease process, although statins exert beneficial effects beyond lowering serum lipids (Shirinsky & Shirinsky, 2007).

Adhesion molecules.

Increased expression of cellular adhesion molecules, such as intracellular adhesion molecule-1 and vascular cell adhesion molecule-1, has been hypothesized to be an important component of psoriasis pathology through trafficking of immunologic cells into the skin (Cabrijan, Batinac, Lenkovic, & Gruber, 2009). For example, intracellular adhesion molecule-1 expression was prominent on the vascular epithelium of psoriasis patients even after treatment with cyclosporine, which could potentially explain the rapid recurrence of psoriasis lesions usually seen after the withdrawal of cyclosporine (Horrocks, Duncan, Oliver, & Thomson, 1991). In regards to psoriasis cardiometabolic co-morbidities, increased levels of as intracellular adhesion molecule-1 and vascular cell adhesion molecule-1 are associated with metabolic syndrome (Bonora et al., 2003) and prospectively with the development of CAD (Luc et al., 2003; Schmidt, Hulthe, & Fagerberg, 2009).

Chronic exercise training reduced the expression of circulating adhesion molecules in an animal model (Yang & Chen, 2003) and in patients with T2D and impaired glucose tolerance (Tönjes et al., 2007; Zoppini et al., 2006). The finding that Efalizumab (a highly efficacious anti-psoriasis agent) blocks lymphocyte function-associated antigen binding to intracellular adhesion molecule-1 provides additional support for this potential mechanism (Li et al., 2009).

In summary, a variety of shared mechanisms exist by which psoriasis severity and its cardiometabolic co-morbidities could exacerbate one-another. Inflammatory cytokines, oxidative stress, serum lipids, and adhesion molecules are characteristically altered in psoriasis, CAD, T2D, and metabolic syndrome, and thus, should be targets of future study to delineate their contribution to the pathogenic burden of psoriasis. Additionally, these shared mechanisms suggest PA could positively modify clinical psoriasis severity and its cardiometabolic co-morbidities. These data must be interpreted with caution, as all these potential mechanisms are speculative. They do, however, serve as a theoretical basis for studying the physiological effects of PA in psoriasis.

Evidence supporting the hypothesis of a negative association between psoriasis severity and physical activity.

The social stigma associated with psoriasis—whether perceived or real—may make it particularly problematic for patients to adhere to regular PA. Social activities are commonly avoided by psoriasis sufferers. A survey of 104 individuals with psoriasis demonstrated wide-spread social avoidance behaviors, including avoidance of activities and places common to exercise and PA (Ramsay & O'Reagan, 1988). Forty percent reported avoiding sports, 64% avoided communal showers, and 64% avoided wearing shorts or short-sleeved shirts. Most disturbingly, 11.5% avoided leaving their own home. Many of these avoidance patterns may originate from the manner in which psoriasis patients believe they are perceived by others. In the same survey, 57% felt as though others stared at them and 56% thought of their bodies as unclean (Ramsay & O'Reagan, 1988). Many of these results were not exclusive to patients with severe disease; even mild psoriasis sufferers reported social avoidance behaviors and disturbances in psychological thoughts. Another study by Koo (1996) showed that of all day-to-day activities (being interviewed, courtship, giving a presentation, going to a barber, sexual activities, shaking hands, etc.), going to a pool, beach, or gym caused the most anxiety for psoriasis patients.

Beyond the social and psychological barriers to PA that psoriasis confers, other physiologic barriers may make PA more difficult in psoriasis. Leibowitz, Seidman, Laor, Shapiro, and Epstein (1991) had sixteen young male patients with psoriasis perform an exercise test in hot and humid conditions. As compared to non-psoriatic controls, subjects with psoriasis were less effective at dissipating heat over 2-hours of exercise in 40º Celsius, 40% relative humidity conditions. Controls had higher total body sweat rates, allowing them to dissipate heat at a greater rate. It appeared that psoriasis lesions interfered with normal sweating, and indeed, the sweat rates for both groups were proportional to the amount of healthy skin. Subjects with psoriasis had higher heart rates over the test (137 versus 120 beats per minute after 2 hours), indicating that they may not be able to tolerate the same absolute level of exercise intensity in hot and humid conditions (Leibowitz et al., 1991).

These data provide some tenuous support that individuals with psoriasis may be less likely to engage in regular PA, especially structured exercise. No direct evidence exists,

however, to support this hypothesis. Unfortunately, the attitudes, perceptions, and behaviors toward PA have not been systematically studied in patients with psoriasis.

Evidence supporting the hypothesis of a positive association between physical activity and quality of life in psoriasis.

A systematic literature review from de Korte et al. (2004) on psoriasis and QOL issues indicated that normal daily activities such as walking, climbing stairs, and daily work were negatively affected by psoriasis, and patients also experienced feelings of reduced vitality and increased fatigue. Although psoriasis severity tends to predict decrements in QOL, these two variables do not correlate strongly, with coefficients typically ranging between 0.15-0.40 (Fortune, Main, O'Sullivan, & Griffiths, 1997a; Samponga, Sera, & Abeni, 2004). In addition, treatment-induced decreases in physician-assessed disease severity do not always correlate strongly with improvements in QOL (Touw et al., 2001).

Despite the lack of a consistent association between disease severity and QOL, a number of studies have shown that reductions in psoriasis severity from pharmacological treatments improve QOL (Sergay, Silvan, & Weinberg, 2008). One study with the systemic drug alefacept in patients with moderate-to-severe psoriasis found that at least a 50% reduction in physical lesions was required for significant improvements in several QOL parameters (Ellis, Mordin, & Adler, 2003).

The effects of non-pharmological treatments on QOL—such as PA, diet, psychotherapy, alcohol/smoking interventions, weight loss—have not been studied extensively in psoriasis (Sergay, Silvan, & Weinberg, 2008). A few examples from the literature, however, demonstrate the potential usefulness of these non-pharmological interventions. A comprehensive disease management program implemented at ten dermatology centers in several European countries evaluated QOL changes in patients with mild-to-moderate psoriasis (de Korte, Van Onselen, Kownacki, Sprangers, & Bos, 2005). The program involved three face-to-face consultations over two months utilizing disease education, disease management training, and psychological support; the patients were also being treated with topical medications. After two months, patients improved their adherence to medications, experienced decreases in disease severity, and improved their QOL. Overall satisfaction with the program was high, as 99% of the patients

would recommend the program to others with psoriasis. Unfortunately, no control group was used in this particular study.

Another study evaluated the effectiveness of a six week adjunctive cognitive-behavioral therapy (CBT) program in comparison to standard care on psoriasis severity and disability measures (Fortune et al., 2002). The CBT program aimed to help psoriasis patients identify and manage inappropriate beliefs and perceptions regarding their psoriasis. Patients chose either to participate in the CBT program or to receive standard care, and those that chose the CBT program attended six, 2.5-hour small group sessions over the course of the study. Patients in the CBT program showed statistically significant effects compared to standard care in regards to disease severity, anxiety, depression, and psoriasis-related stress at both the end of the CBT program and at 6 months follow-up (Fortune et al., 2002).

Evidence from a wide-range of chronic diseases suggests that PA often relates to and can improve QOL in populations with a reduced QOL. Studies from chronic heart failure (Belardinelli, Georgiou, Cianci, & Purcaro, 1999), multiple sclerosis (Schulz et al., 2004), systemic lupus erythematosus (Carvalho et al., 2005), Crohn's disease (Ng, Millard, Lebrun, & Howard, 2007), kidney failure with hemodialysis (Painter, Carlson, Carey, Paul, & Myll, 2000), and post-treatment breast cancer (Courneya et al., 2003) all provide evidence that PA and exercise beneficially affect QOL. The aforementioned conditions, though, are characterized by significant fatigue, which has not been systematically documented in psoriasis populations.

Psoriasis presents unique challenges because of its multi-faceted manifestations and causes both physical and psychological detriments to QOL. QOL is predicted by psoriasis disease severity, but only modestly so. Therefore, it is imperative to examine what other factors, such as PA, may be associated with QOL in psoriasis.

Conclusion

Psoriasis is a chronic, incurable disease of the skin resulting from abnormalities in skin cell proliferation and differentiation. These abnormalities are primarily driven by disturbances in the immune system and through the increased expression of several inflammatory cytokines.

Psoriasis can severely impact QOL. Sufferers often struggle to deal with the stigma and physical discomfort psoriasis generates. Individuals with psoriasis are at greater risk for psychosocial disturbances. In addition, psoriasis sufferers may be at increased risk for serious

and potentially life-threatening cardiometabolic co-morbidities such as CVD, T2D, obesity, and metabolic syndrome.

PA is an effective primary and adjunctive treatment in many chronic diseases; unfortunately, only a handful of studies have examined the PA patterns of people with psoriasis, and no study to date has related PA to disease severity or QOL in psoriasis. There is a clear need to scientifically evaluate PA in patients with psoriasis and to quantify its association to disease severity and QOL. Lifestyle behaviors such as PA are uniquely suited to improve functioning and QOL in many individuals with minimal risk of side-effects.

Chapter 3: Methodology

Study Design

The study used a cross-sectional design to examine the associations between self-assessed psoriasis severity, self-reported PA, and self-reported QOL. The cross-sectional design is justified, as information on the associations between these parameters is absent from the literature. In addition, the use of questionnaires made the data collection relatively unobtrusive to the participants and limited the reliance on other health professionals (Creswell, 2009).

Population and Sample

The target population consisted of individuals with any form of chronic psoriasis. In the United States, approximately 2-3% of the population is afflicted with psoriasis (Koo, 1996; Stern et al., 2004). Sampling of individuals with psoriasis was done via a convenience sample. Study participants were recruited from the Minnesota Psoriasis Support Group, the University of Minnesota Dermatology Clinic, and by posting fliers on college campuses. Approximately 250 letters were mailed to listed members of the Minnesota Psoriasis Support Group in January of 2011. Fliers (Appendix B) were posted at the University of Minnesota, Macalester College, Hamline University, University of St.Thomas, and St. Cloud State University from February-May of 2011. The following criteria for participation in the study was implemented:

Inclusion criteria.

- ✓ 18-64 years of age
- ✓ Self-reported physician diagnosed psoriasis for at least 1 year

Exclusion criteria.

- ✓ Younger than 18 and older than 64 years of age
- ✓ Self-reported physician diagnosed psoriasis for less than 1 year

The goal sample size was $n = 37$. This estimation was based on a projected negative correlation of $r = 0.40$ between PA and psoriasis severity and a positive correlation of 0.40 between QOL and PA (Koltyn, 2001), using a power = 0.80 and a one-sided $\alpha = 0.05$. No data exists on the association between PA and psoriasis severity, but studies of other lifestyle factors,

such as alcohol use, have found significant correlations (r = 0.27) with disease severity (Kirby et al., 2008).

Variables and Instrumentation

Psoriasis severity.

The advantages and disadvantages of various clinical tools utilized for assessing psoriasis severity have been outlined in recent reviews (Feldman & Krueger, 2005; Spuls et al., 2009). Overall, no consensus has emerged regarding which tool is superior, and the selection of an instrument largely depends on the purpose of the study. The Psoriasis Area and Severity Index (PASI) is the most extensively studied psoriasis severity assessment tool (Puzenat et al., 2010) and shows comparable or greater intra- and inter-rater intraclass correlation coefficients (> 0.80) compared to other assessment tools (Berth-Jones et al., 2006). In addition, it provides a continuous score for analysis. For the proposed study, the Self-Administered Psoriasis Area and Severity Index (SAPASI) was chosen because it does not require a dermatologist for assessment and its high validity compared to the dermatologist measured PASI (Fleischer, Rapp, Reboussin, Vanarthos, & Feldman, 1994). (Note: the SAPASI is not included in the appendices because of copyright restrictions.) In a linear regression model based on a sample of 80 psoriasis patients, the SAPASI explained 59% of the variability from PASI scores (Feldman et al. 1996), indicating it is a valid substitute for the PASI.

The SAPASI provides a pictorial outline of a human body, which allowed study participants to shade in the areas of their body covered by psoriasis. Next, participants used three linear visual analog scales to rate the symptoms of redness, thickness, and scaling.

To score the SAPASI, the body is divided into four regions: (1) the head, (2) the arms, (3) the trunk, and (4) the legs. For each of these regions, I selected out of seven ranges for percent skin involved for that region. Estimation of total BSA between different raters is high using this methodology, with r = 0.95 (Feldman et al., 1996). In addition, agreement between dermatologist and non-dermatologist estimation of BSA is high (r = 0.95) (Feldman et al., 1996). Finally, I graded the severity of three clinical signs (redness, thickness and scaling) by measuring the distance of the mark on the linear visual analog scales made by the participant. These values were then used to calculate a composite score that can range from 0-72.

In addition to the SAPASI, the following statement from Dommasch, Shin,Troxel, Margolis, & Gelfand (2009) was included on the Demographic Questionnaire (Appendix A) in order to estimate the BSA covered by psoriasis.

> "If you had to take the palm of your hand and cover up all of the patches of psoriasis on your body today, how many palms of your hand do you think that it would take? One palm of your hand is equal to about 1% of your body surface area. If your psoriasis is only scattered small dots, try to imagine combining them together into one patch. Please remember to include your scalp and back if affected. Do not include areas in which psoriasis has faded, leaving only changes in the color of the skin."

This question was included in order to compare how BSA alone relates to PA, as opposed to the SAPASI, which is a composite severity index utilizing BSA as well as the symptoms of redness, thickness, and scaling. These comparisons assisted in the determining whether BSA or a composite index of psoriasis symptoms relate most to PA. The validity of using this statement to assess BSA is high, with an intraclass correlation coefficient of 0.81 in comparison to physician assessment (Dommasch et al., 2009).

Physical activity.

Data on PA was collected with the International Physical Activity Questionnaire (IPAQ) (Appendix A). The IPAQ was developed in 1998 out of need for a valid and reliable means of easily quantifying PA in several domains of life (Hagströmer, Oja, & Sjöström, 2006). The IPAQ assesses PA in five domains of life: (1) during transportation, (2) at work, (3) during household tasks, (4) during leisure time activities such as exercise and sport participation, and (5) during time spent sitting. Short and long forms of the IPAQ are available, and the long form (31 questions) was used in this study because of its slightly higher validity and reliability. The results from a 12-country study demonstrated Spearman's rho correlations of 0.81 for repeat reliability and 0.33 for validity against accelerometer, using total PA as the variable of interest (Craig et al., 2003). Validity of the IPAQ against activity monitors and log books among the various activity intensities typically show differences in validity, with vigorous intensity activities showing higher correlations than moderate intensity activities (r = 0.63 vs. 0.12) (Hagströmer, Oja, & Sjöström, 2006). Time spent sitting, PA at work, and leisure-time PA domains show higher validity than PA at home and transportation PA (Hagströmer, Oja, & Sjöström, 2006).

The IPAQ measures recent PA participation, as it asks about PA within the last seven days. Since psoriasis severity can change substantially even within a short period of time, it was important to use a PA instrument that quantified PA in relation to current psoriasis severity.

Continuous scores can be generated as minutes of specific activities or by multiplying the metabolic equivalent (MET) of each activity by the time spent in each activity to generate MET-minutes/week for total PA and domain specific PA. The current study used MET-minutes/week because it incorporates both time and intensity information into one continuous score.

Quality of life.

Starting 1991, the World Health Organization Quality of Life (WHOQOL) initiative began with the aim of developing cross-culturally comparable QOL instruments. The proposed study used one of these instruments, known as the WHOQOL-BREF (Appendix A), which comprises 26 questions that measure QOL in the following domains: (1) physical health, (2) psychological health, (3) social relationships, and (4) environment ("Development of," 1998). Scores from each question are added together and can be transformed to a scale between 0-100. The WHOQOL-BREF has shown good-to-excellent reliability and is a valid measure of QOL in both sick and healthy populations (Skevington, Lotfy & O'Connell, 2004).

In addition to using a generic QOL instrument, the current study utilized a skin-disease specific QOL questionnaire. The Dermatology Life Quality Index (DLQI) (Appendix A), which was originally developed in 1994, was used in the current study because it is one of the most widely used dermatology QOL indexes and has good-to-excellent reliability and validity properties (Finlay & Khan, 1994; Shikiar, Willian, Okun, Thompson, & Revicki, 2006). Furthermore, it consists of only 10 questions, which lowered the burden of effort for participants. Participants rate how much they agree with each question from not at all to very much (0-3). The scores from each question are added together to range from 0-30, with a higher score indicating greater impairment to QOL.

Additional variables.

Additional data was collected to help assess the nature of the sample. The Demographic Questionnaire asked about age, sex, race/ethnicity, education, psoriasis duration, PsA diagnosis, PsA duration, and any current treatments being used.

To help assess whether PA was associated with psoriasis severity independent of other factors, data on a number of other variables was collected. Excessive weight is a known predictor of psoriasis severity (Herron et al., 2005; Setty, Curhan, & Choi, 2007), and PA is inversely associated with weight and BMI (Erlichman, Kerbey, & James, 2002). Weight was measured using a digital scale (Taylor Precision Products, Las Cruces, NM) and height was self-reported. BMI was calculated using the formula kg/m^2.

Both smoking and alcohol use are negatively associated with PA (Lahti-Koski, Pietinen, Heliövaara, & Vartiainen, 2002; Sneve & Jorde, 2006), so data on both was assessed on the Demographic Questionnaire. Participants were asked whether they have regularly smoked during the past 6 months, and if so, to estimate approximately how many cigarettes per day they smoked during the past 6 months. Smoking was quantified as a continuous variable as the average number of cigarettes smoked per week. Previous research has related cigarettes smoked in the past 6 months to psoriasis severity (Gupta, Gupta, & Watteel, 1996).

To assess drinking habits, participants were asked to indicate how frequently they consumed several types of alcoholic beverages, including light beer, regular beer, wine or champagne, and liquor. For the purpose of data analysis, a standard drink of 12 ounces (oz) of beer, 4 oz of wine or champagne, or 1.5 oz of liquor was considered equivalent to 14 grams (g) of alcohol (Centers for Disease, 2010). This general approach utilizing frequency and quantity questions to measure alcohol consumption has shown satisfactory reliability and validity for observational research (Del Boca & Darkes, 2003).

Ethical Considerations

Prior to initiating any contact with potential participants, approval to conduct human research was obtained from the University of Minnesota Institutional Review Board. In addition, I completed human subject research training via the Collaborative Institutional Training Initiative through the University of Minnesota.

Before any data collection occurred, I described the following topics to each participant: the study purpose, procedures to be done, potential risks and discomforts, any benefits to be gained, confidentiality protection, voluntary nature of the study, and where to address questions or complaints. The participant was then allowed adequate time to review the written Informed Consent (Appendix B) and was encouraged to ask questions. If the participant wished to participate, they were asked to sign and date the Informed Consent document. A signature was also obtained from the individual conducting the informed consent process and a copy was given to the participant.

Procedures for Data Collection

Potential participants contacted me via email or telephone from the provided contact information on advertisement materials. During the initial contact, I briefly described the purpose and procedures of the study. If interested, the potential participant was asked to come to the Laboratory of Physiological Hygiene and Exercise Science (LPHES) at the University of Minnesota. If the participant was not willing or able to come to the LPHES, I volunteered to travel to their residence.

The data was collected in a quiet, private office at the LPHES or in the room of choice at the participant's residence. Participants first filled out the Demographic Questionnaire. Next, the participants completed the IPAQ, WHOQOL-BREF, DLQI and SAPASI questionnaires. Finally, a weight was taken with the participant clothed but without shoes. In general, most participants needed 25-30 minutes to complete the study requirements.

Once the data had been collected, I scored the SAPASI, IPAQ, WHOQOL-BREF, and DLQI. The SAPASI was scored first because it involves some subjective rating and was most vulnerable to bias. Thus, I did not have knowledge of any PA or QOL data prior to scoring the SAPASI. Data from these instruments, along with data from the Demographic Questionnaire, was then inputted into spreadsheets for future analysis.

Study Hypotheses

The following primary hypotheses were formed prior to data collection and were used to guide the final analysis:

1. Total PA is negatively associated with BSA.

2. Total PA is negatively associated with SAPASI scores.
3. Leisure PA is negatively associated with BSA.
4. Leisure PA is negatively associated with SAPASI scores.

The remaining analysis, as discussed below, was dictated by the results obtained from these four hypotheses.

Statistical Analysis

Statistical analysis was performed using PASW Statistics 18 software program (SPSS Inc, Chicago, IL). Spearman's rho correlations were performed between continuous/ordinal variables because of the non-normal distribution seen with PA and psoriasis severity data. First, SAPASI scores and BSA involvement were correlated with total and leisure PA quantified as MET-minutes/week. One-tailed values at the $p<0.05$ level (negative associations) were considered significant for these correlations. The analysis was limited to these variables in order to minimize the problem of multiple comparisons and because people generally have more control over leisure PA as compared to other PA domains such as work and transportation. Only the most highly correlated PA domain (total or leisure) was included in further analyses. Additional demographic variables correlated against PA were considered significant using a two-tailed cutoff of $p<0.05$. Two-tailed tests were used for these correlations because the current study did not hypothesize as to the direction of these associations.

For dichotomous variables such as sex or PsA diagnosis, the Mann-Whitney-Wilcoxon test was used to assess differences in PA scores between groups. The Mann-Whitney-Wilcoxon test is preferred when data tends to be non-normally distributed (Delucchi & Bostrom, 2004), such as with PA data.

Finally, PA was correlated with the physical and psychological domains from the WHOQOL-BREF and the total DLQI score. In addition, scores from question 1 from the DLQI, "Over the past week, how itchy, sore, painful, or stinging has your skin been?" were correlated with PA. This was done to help differentiate the effects of BSA from other symptoms on PA. One-tailed values $p<0.05$ were considered significant; positive associations between the WHOQOL-BREF variables and PA were expected while negative associations between DLQI variables and PA were expected.

Chapter 4: Results

Sample Demographics

Twenty-three individuals met the inclusion criteria and completed the necessary requirements of the study. Descriptive information for various sociodemographic characteristics is presented in Table 1 for the overall sample and by sex. The average participant age was 40.2 years. Fourteen of the participants were female (60.9%) and 20 were white (87.0%). The average participant was overweight with a BMI of 27.1, and women had a higher average BMI than men. Participants were generally well-educated since most had at least a two-year college degree. Only two of the participants were smokers (8.7%), while 60.9% of the participants reported drinking alcohol. A slightly greater proportion of men reported drinking, and among drinkers, the average was much higher for men (181.0 vs. 15.7 g/week).

Table 1: Demographic Characteristics

	Overall (n=23)		**Women (n=14)**		**Men (n=9)**	
	%	**Mean (SD)**	**%**	**Mean (SD)**	**%**	**Mean (SD)**
Age (years)		40.2 (15.5)		39.1 (14.9)		42.0 (17.1)
Ethnicity/Race						
White	87.0		92.9		77.8	
Hispanic	8.7		0		22.2	
Asian	4.3		7.1		0	
Height (cm)		172.0 (9.1)		166.6 (5.8)		180.2 (6.3)
Weight (kg)		79.6 (13.7)		78.2 (14.1)		81.9 (13.5)
BMI (kg/m^2)		27.1 (5.5)		28.3 (6.3)		25.1 (3.3)
Education (1-8)		4.5 (1.7)		4.2 (1.6)		5 (1.7)
Smoker	8.7		7.1		11.1	
Cigarettes/week[a]		80.5 (34.6)		56 (0)		105 (0)
Drinker	60.9		57.1		66.6	
Alcohol (g/week)[b]		87.2 (158.6)		15.7 (11.1)		181.0 (216.2)

a. Averages shown are among smokers with non-smokers excluded.
b. Averages shown are among drinkers with non-drinkers excluded.

In regards to psoriasis disease characteristics, the average length of time since reported diagnosis of psoriasis was 22.9 years. Approximately 80% of the sample had either mild-to-moderate disease (<10%) defined by BSA, while one-fifth had severe disease (>10% BSA). Six of the participants reported being diagnosed with PsA (26.1%) for an average of 10.5 years since

their diagnosis. Almost half (43.5%) of the participants reported using no treatments, 26.1% reported using topical treatments alone, and 30.4% reported using systemic treatments or a combination of system and topical treatments. The psoriasis disease characteristics of the overall sample and by sex are presented in Table 2.

Table 2: Psoriasis Disease Characteristics

	Overall (n=23)		**Women (n=14)**		**Men (n=9)**	
	%	**Mean (SD)**	**%**	**Mean (SD)**	**%**	**Mean (SD)**
Psoriasis Duration (years)		22.9 (13.7)		23.3 (11.8)		22.1 (16.9)
PsA Diagnosis	26.1		35.7		11.1	
PsA Duration (years)		10.5 (13.5)		12.2 (14.3)		2.0 (0)
BSA Involvement (%)		11.9 (21.5)		16.3 (26.7)		5.2 (6.1)
BSA Classification						
Mild (<3%)	39.1		35.7		44.4	
Moderate (3-10%)	39.1		35.7		44.4	
Severe (>10%)	21.7		28.6		11.1	
Treatment Classification						
None	43.5		50.0		33.3	
Topical Only	26.1		21.4		33.3	
Systemic or Combination	30.4		28.6		33.3	

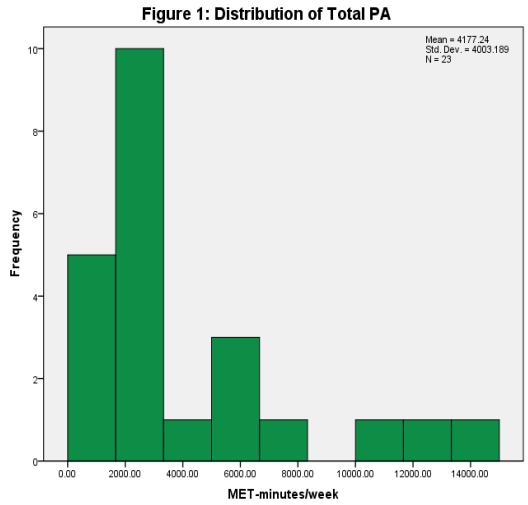
Associations between Physical Activity, SAPASI, and Other Demographic Data

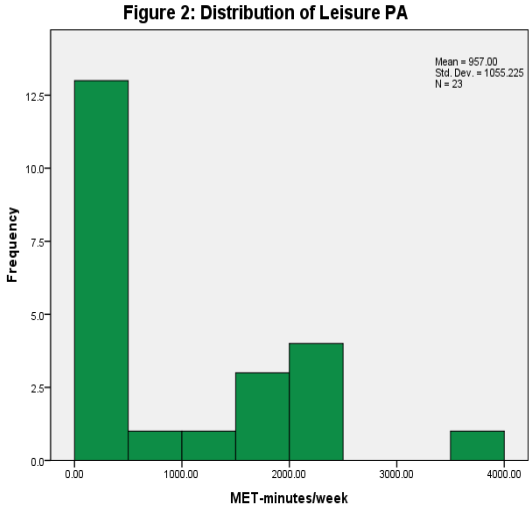
The distributions of total PA, leisure PA, SAPASI scores, and BSA involvement are shown in Figures 1-4. All demonstrate a non-normal distribution with a substantial proportion of the data being at the lower end of PA and psoriasis severity. Additional PA data from each domain of the IPAQ, quantified as both MET-minutes/week and minutes/week, can be seen in Appendix C.

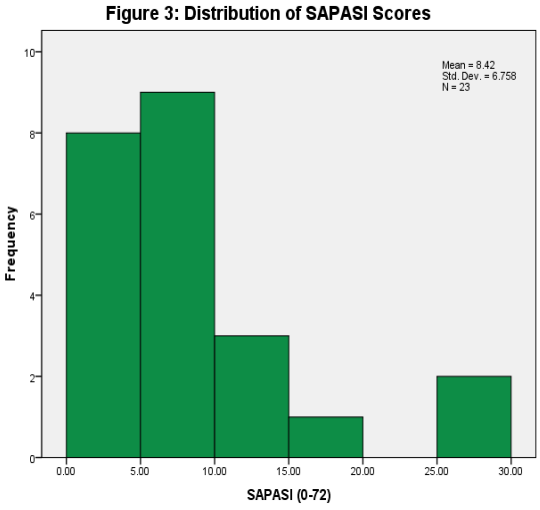
Total PA as MET-minutes/week was not significantly negatively correlated with either SAPASI scores (r=-0.008, p=0.49) or BSA (r=0.232, p=0.14). Leisure PA, however, showed a significant negative correlation with SAPASI scores (r=-0.602, p=0.001), but not with BSA (r=-0.191, p=0.19). These correlations are shown in Table 3.

Figures 5 is a scatterplot of leisure PA vs. SAPASI scores, and by visually inspecting the data, three data points appeared to be potential outliers. Figure 6 shows the same scatterplot with these three data points removed. Re-analysis of the reduced data (n=20) did not appreciably change the Spearman's rho for leisure PA and SAPASI scores (r=-0.663, p=0.001).

Based on these initial analyses, leisure PA for all data points was correlated against several other factors, including age, psoriasis duration, BMI, and education. None of these variables were significantly correlated with leisure PA, although education did show a modest positive association (r=0.300, p=0.16). These correlations are shown in Table 3.







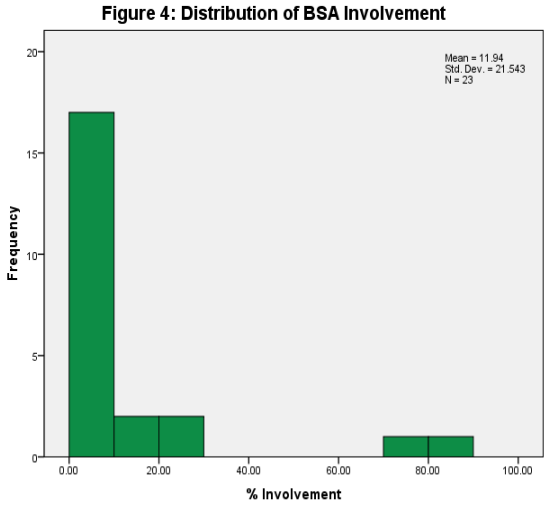


Table 3: Correlations Among Selected Variables and PA Scores (n=23)

	Total PA (MET-minutes/week)		**Leisure PA (MET-minutes/week)**	
	Spearman's rho	**p-value**	**Spearman's rho**	**p-value**
SAPASI (0-72)	-.008	.486	-.602*	.001
BSA (0-100)	.232	.143	-.191	.191
Age (years)			.046	.834
Psoriasis Duration (years)			-.063	.775
BMI (kg/m^2)			-.019	.932
Education (1-8)			.300	.164

Note: SAPASI and BSA were one-tailed tests; Age, Psoriasis Duration, BMI, and Education were two-tailed tests.
*. Correlation significant at the 0.01 level (1-tailed).

Figure 5: Scatterplot of Leisure PA vs. SAPASI Scores

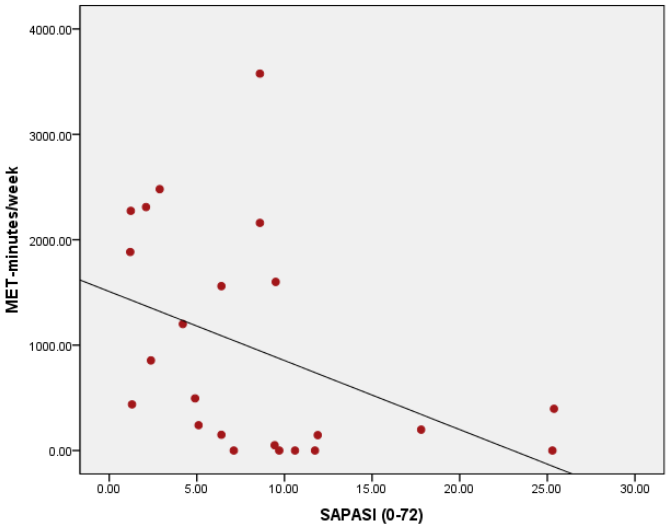
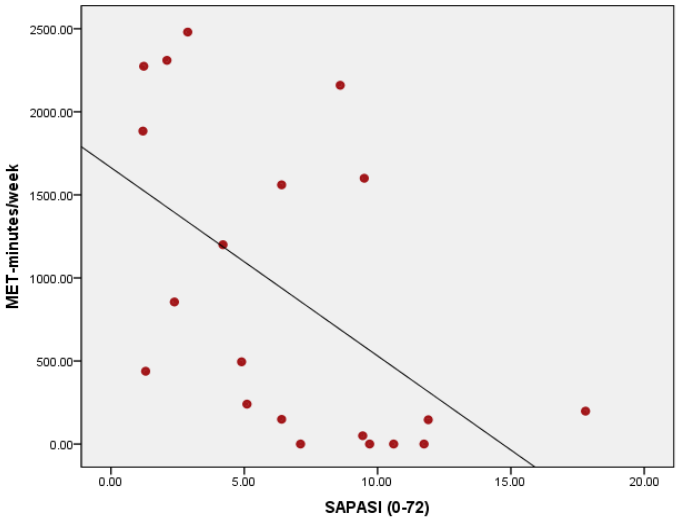


Figure 6: Scatterplot of Leisure PA vs. SAPASI Scores (Reduced Plot)



The results of the Mann-Whitney-Wilcoxon tests indicated between-group differences for the sexes, with men being more physically active in their leisure time than women (p=0.02). Overall, the average amount of leisure PA was 1584 MET-minutes/week for men and 554 MET-minutes/week for women. Leisure PA appeared to differ by PsA diagnosis (274 vs. 1198 MET-minutes/week), but this trend failed to reach statistical significance (p=0.10), likely in part due to only six participants having PsA. These results can be seen in Table 4.

Table 4: Differences in Leisure PA Between Dichotomous Factors (n=23)

	Sex		**PsA Diagnosis**	
	Male	**Female**	**Yes**	**No**
Leisure PA (MET-minutes/week)	1584.3	553.7	274.2	1198.0
	Mann-Whitney U 26.0	p-value .019[a]	Mann-Whitney U 27.0	p-value .101[a]

a. Not corrected for ties.

Associations between Physical Activity and Quality of Life

Neither the physical or psychological domains from the WHOQOL-BREF demonstrated a significant positive association with leisure PA, even though the correlation for the psychological domain was modest (r=0.232, p=0.14).

A modest negative correlation (r=-0.250, p=0.13) existed between the total DLQI score and leisure PA. Question 1 from the DLQI, however, exhibited a strong negative correlation (r=-0.662, p<0.001) with leisure PA, indicating that symptoms of itching, soreness, stinging, and pain are important factors related to leisure PA. These results are presented in Table 5.

Table 5: Correlations Among QOL Variables and Leisure PA (n=23)

	Leisure PA (MET-minutes/week)	
	Spearman's rho	**p-value**
WHOQOL-BREF Physical (0-100)	.033	.441
WHOQOL-BREF Psychological (0-100)	.232	.144
DLQI Total (0-30)	-.250	.125
DLQI Question 1 (0-3)	-.662*	.000

*. Correlation significant at the 0.01 level (1-tailed).

Chapter 5: Discussion

These results demonstrate that disease severity as measured by the SAPASI is negatively associated with leisure PA, but not total PA, in individuals with psoriasis. Several potential factors may explain this phenomenon. Since individuals may have more control over leisure PA, their willingness to participate in leisure PA may be more susceptible to differences in psoriasis severity. Differences in the validity of these measures may have also contributed to the findings. The higher validity of leisure PA than total PA when using the IPAQ may have contributed to the strength of the observed associations (Hagströmer, Oja, & Sjöström, 2006).

Another significant finding of this study was that psoriasis severity as measured by BSA alone was not strongly associated with leisure PA. It is unlikely that these results can be explained by differences in the methods used to quantify psoriasis severity. Both the BSA and SAPASI scores relied on the participant's ability to assess their psoriasis severity. What's more, the method used to quantify BSA actually has shown higher validity and reliability than the SAPASI in previous research (Dommasch et al., 2009; Feldman et al., 1996). Despite its lower validity and reliability, the SAPASI scores were more strongly associated with leisure PA. Additionally, a single question from the DLQI asking about pain, stinging, soreness, and itching showed a strong negative association with leisure PA, further supporting the notion that BSA alone may be a weak correlate of leisure PA.

Other potential factors could explain the observed associations between leisure PA and psoriasis severity. Participants with PsA engaged in less leisure PA than non-PsA participants (274 vs. 1198 MET-minutes/week), which agrees with previous research demonstrating reduced PA in adults with arthritis (Shih, Hootman, Kruger, & Helmick, 2006). Unfortunately, the small number of participants did not allow for the examination of PsA as a part of a multivariate adjusted model. Moreover, the current study did not assess factors such as PsA severity or the location of affected joints that could relate to leisure PA participation.

While the current study establishes an association between leisure PA and psoriasis severity, it is not possible to determine the direction of the association. The visual lesions of psoriasis may cause psychosocial impairments that contribute to decreased leisure PA. Likewise, physical symptoms such as pain, stinging, soreness, and itching may make PA and exercise uncomfortable endeavors. Alternatively, a low level of leisure PA may contribute to a worsening

of psoriasis symptoms by a number of mechanisms, such as increased oxidative stress and inflammation.

Another aim of the current study was to evaluate the associations between PA and QOL in psoriasis. The psychological domain of the WHOQOL-BREF showed a modest positive association with leisure PA while the physical domain showed a weak association with leisure PA. These results are somewhat at odds with some previous research in non-psoriasis populations showing physical QOL to be more strongly correlated with PA than psychological or mental QOL (Koltyn, 2001; Laforge et al., 1999; Shibata, Oka, Nakamura, & Muraoka, 2007). Evidence from psoriasis populations, however, has demonstrated that psychological distress is often a stronger predictor of functioning and disability than objective psoriasis severity (Fortune et al., 1997b; Fortune, Richards, Griffiths, & Main, 2002), and it is plausible that this extends to participation in leisure PA.

Total scores from the DLQI showed a modest negative association with leisure PA. Higher scores on the DLQI indicate a greater level of QOL impairment. The ten questions from the DLQI cover several aspects of QOL and can be considered a global measure of QOL. Since question 1 from the DLQI demonstrated such a strong negative association with leisure PA, the possibility exists that any improvement in the DLQI with leisure PA would depend highly on how it would affect symptoms such as pain, stinging, soreness, and itching

Limitations

A primary limitation of this study was the relatively small sample size, as the original goal of n=37 was not achieved. Furthermore, the number of statistical comparisons used in the study creates the possibility of spurious significant associations. However, the exploratory nature of the study makes this an acceptable risk. In addition, an attempt was made to limit the number of statistical comparisons done as a part of the analysis.

Differing distributions of variables known to affect psoriasis severity may be present among individuals with varying levels leisure PA, and thus, could confound the association between psoriasis severity and leisure PA. To evaluate these threats to validity, information on potentially confounding variables was collected and correlated against leisure PA to explore these potential associations. Age, BMI, and psoriasis duration showed very weak associations

(r<0.1) with leisure PA. Education, sex, and PsA diagnosis appeared to be potential confounders and should be targets for evaluation in the future.

The questionnaires that were used also pose threats to validity (Creswell, 2009). All the questionnaires have been validated previously and were presented to the participants with the same instructions. Ultimately, though, the validity of any questionnaire-based assessment of PA and psoriasis severity is limited.

Finally, the convenience sample used in the current study may not reflect the average person with psoriasis. Individuals from a psoriasis support group are likely different from those who do not seek this form of support. Moreover, most fliers were posted on college campuses, and this may have led to a more educated sample. Indeed, the average amount of education was between a two- and four-year college degree. Despite this, the study sample does mirror those from other national-wide psoriasis samples. Eighty-seven percent of the study sample was white, which compares to the 90% that other studies in the United States have generally found (Stern et al., 2004). Psoriasis severity defined by BSA was similar to that seen in national samples, but in the current study there was a slightly higher proportion of severe cases (21% vs. 10%) (Koo, 1996; Stern et al., 2004). In a survey from 1,657 National Psoriasis Foundation members with moderate-to-severe psoriasis, approximately 40% were not receiving any form of treatment, which is similar to the 43.5% in the current study (Horn, Fox, Patel, Chiou, Dann, & Lebwohl, 2007a). Additionally, 26.1% of the participants reported having PsA, which falls within the 6-42% range seen in the literature (Gladman et al., 2005).

Chapter 6: Conclusion

The results of the current exploratory study provide evidence that psoriasis severity is negatively associated with leisure PA. Furthermore, a combination of skin symptoms including BSA involvement, redness, itching, and thickness demonstrates a stronger association with leisure PA than BSA alone. Reduced leisure PA in individuals with moderate-to-severe psoriasis could account for some of the increased risk of cardiometabolic co-morbidities such CVD, T2D, obesity and metabolic syndrome seen in this population. Future studies should continue to explore the associations between PA and psoriasis severity. Additional cross-sectional studies with larger sample sizes and more objective measures of PA should be undertaken to confirm these initial results. In addition, prospective and interventional studies are needed to clarify what effects increasing PA would have on psoriasis severity, QOL, and the risk of cardiometabolic co-morbidities. Psoriasis is an incurable disease that can cause both physical and psychosocial decrements to health. PA is uniquely suited to improve health and functioning in many individuals and it is imperative that we gain a better understanding of its effects in psoriasis.

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Appendix A: Questionnaires

Demographic Questionnaire

Name:_____ Age:_____ Sex: M F

Race:
_____white
_____African-American
_____Hispanic
_____Asian-Pacific Islander
_____Native American
Other, specify:_____

What is the highest level of education you have completed? Please check one.
_____ Less than high school education
_____ High education/GED
_____ Some college
_____ 2-year college degree (associate's degree)
_____ 4-year college degree (BA, BS)
_____ Master's degree
_____ Doctoral degree
_____ Professional degree (MD, JD)

Psoriasis Information:

Is your psoriasis plaque psoriasis? Y N Not sure

Was your psoriasis diagnosed by a physician (family doctor, dermatologist, etc)? Y N

Approximately how long have you had psoriasis? _____years _____months

Have you ever been diagnosed with psoriatic arthritis? Y N When?_____

If you had to take the palm of your hand and cover up all of the patches of psoriasis on your body today, how many palms of your hand do you think that it would take? One palm of your hand is equal to about 1% of your body surface area. If your psoriasis is only scattered small dots, try to imagine combining them together into one patch. Please remember to include your scalp and back if affected. Do not include areas in which psoriasis has faded, leaving only changes in the color of the skin'.

Number of palms: _____

Please indicate if you are **currently** using any of the following medications, and if so, how long you have been using it:

Topical:			**How Long?**
Topical steroids……	Y	N	_____
Vitamin D analogue (Dovonex, Vectical, etc)……	Y	N	_____
Combination steroid/vitamin D (Dovobet)……..	Y	N	_____
Vitamin A derivative (Tazorec)…….....	Y	N	_____
Anthralin (Zithranol)……	Y	N	_____

Phototherapy:
UVB phototherapy……...Y N _____
Psoralen + UVA phototherapy (PUVA)……..Y N _____
Excimer laser……....Y N _____
Pulsed dye laser…….**...**Y N _____

Systemic:
Acitretin (Soriatane)……Y N _____
Isotretinoin (Accutane)…….Y N _____
Cyclopsorine (Neoral)……..Y N _____
Methotrexate **(**Rheumatrex, Trexall)……Y N _____

Biologic:
Alefacept (Amevive)……Y N _____
Etanercept (Enbrel)……..Y N _____
Adalimumab (Humira)…….Y N _____
Infliximab (Remicade)…….Y N _____
Golimumab (Simponi)……...Y N _____
Ustekinumab (Stelara)……..Y N _____

Smoking History:

Are you a current smoker? Y N

If yes, approximately how long have you smoked? _____years _____months

If currently smoking, over the past **6 months** on average how many cigarettes have you smoked per day?_____ or per week?_____

Drinking History
Please complete the table below on alcohol drinking habits:

Beverage	**A typical serving size**	**Your typical serving size**	**How often do you drink consume this?** (circle one)
Light beer	12 oz (bottle or can)		1x month 2-3x month 1x week 2-3x week 3-5x week Once per day 2-3x day 4 or more times day

Regular beer	12 oz (bottle or can)		1x month 2-3x month 1x week 2-3x week 3-5x week Once per day 2-3x day 4 or more times day
Wine/champagne	4 oz (half glass)		1x month 2-3x month 1x week 2-3x week 3-5x week Once per day 2-3x day 4 or more times day
Liquor (gin, vodka, whiskey, rum)	1.5 oz (shot)		1x month 2-3x month 1x week 2-3x week 3-5x week Once per day 2-3x day 4 or more times day

Please leave blank:
Weight:_____ Height:_____ BMI:_____

Waist circumference: _____

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE (October 2002)

LONG LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ

The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ

Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation

Translation from English is encouraged to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ

International collaboration on IPAQ is on-going and an ***International Physical Activity Prevalence Study*** is in progress. For further information see the IPAQ website.

More Information

More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective.* Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** and **moderate** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal.

PART 1: JOB-RELATED PHYSICAL ACTIVITY

The first section is about your work. This includes paid jobs, farming, volunteer work, course work, and any other unpaid work that you did outside your home. Do not include unpaid work you might do around your home, like housework, yard work, general maintenance, and caring for your family. These are asked in Part 3.

1. Do you currently have a job or do any unpaid work outside your home?

   ☐ Yes

   ☐ No → ***Skip to PART 2: TRANSPORTATION***

The next questions are about all the physical activity you did in the **last 7 days** as part of your paid or unpaid work. This does not include traveling to and from work.

2. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, heavy construction, or climbing up stairs **as part of your work**? Think about only those physical activities that you did for at least 10 minutes at a time.

   _____ **days per week**

   ☐ No vigorous job-related physical activity → ***Skip to question 4***

3. How much time did you usually spend on one of those days doing **vigorous** physical activities as part of your work?

   _____ **hours per day**
   _____ **minutes per day**

4. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads **as part of your work**? Please do not include walking.

   _____ **days per week**

   ☐ No moderate job-related physical activity → ***Skip to question 6***

LONG LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised October 2002.

5. How much time did you usually spend on one of those days doing **moderate** physical activities as part of your work?

_____ **hours per day**
_____ **minutes per day**

6. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **as part of your work**? Please do not count any walking you did to travel to or from work.

_____ **days per week**

☐ No job-related walking → ***Skip to PART 2: TRANSPORTATION***

7. How much time did you usually spend on one of those days **walking** as part of your work?

_____ **hours per day**
_____ **minutes per day**

PART 2: TRANSPORTATION PHYSICAL ACTIVITY

These questions are about how you traveled from place to place, including to places like work, stores, movies, and so on.

8. During the **last 7 days**, on how many days did you **travel in a motor vehicle** like a train, bus, car, or tram?

_____ **days per week**

☐ No traveling in a motor vehicle → ***Skip to question 10***

9. How much time did you usually spend on one of those days **traveling** in a train, bus, car, tram, or other kind of motor vehicle?

_____ **hours per day**
_____ **minutes per day**

Now think only about the **bicycling** and **walking** you might have done to travel to and from work, to do errands, or to go from place to place.

10. During the **last 7 days**, on how many days did you **bicycle** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No bicycling from place to place → ***Skip to question 12***

11. How much time did you usually spend on one of those days to **bicycle** from place to place?

_____ **hours per day**
_____ **minutes per day**

12. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time to go **from place to place**?

_____ **days per week**

☐ No walking from place to place → ***Skip to PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY***

13. How much time did you usually spend on one of those days **walking** from place to place?

_____ **hours per day**
_____ **minutes per day**

PART 3: HOUSEWORK, HOUSE MAINTENANCE, AND CARING FOR FAMILY

This section is about some of the physical activities you might have done in the **last 7 days** in and around your home, like housework, gardening, yard work, general maintenance work, and caring for your family.

14. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, chopping wood, shoveling snow, or digging **in the garden or yard**?

_____ **days per week**

☐ No vigorous activity in garden or yard → ***Skip to question 16***

15. How much time did you usually spend on one of those days doing **vigorous** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

16. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, sweeping, washing windows, and raking **in the garden or yard**?

_____ **days per week**

☐ No moderate activity in garden or yard → ***Skip to question 18***

LONG LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised October 2002.

17. How much time did you usually spend on one of those days doing **moderate** physical activities in the garden or yard?

_____ **hours per day**
_____ **minutes per day**

18. Once again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** activities like carrying light loads, washing windows, scrubbing floors and sweeping **inside your home**?

_____ **days per week**

☐ No moderate activity inside home → ***Skip to PART 4: RECREATION, SPORT AND LEISURE-TIME PHYSICAL ACTIVITY***

19. How much time did you usually spend on one of those days doing **moderate** physical activities inside your home?

_____ **hours per day**
_____ **minutes per day**

PART 4: RECREATION, SPORT, AND LEISURE-TIME PHYSICAL ACTIVITY

This section is about all the physical activities that you did in the **last 7 days** solely for recreation, sport, exercise or leisure. Please do not include any activities you have already mentioned.

20. Not counting any walking you have already mentioned, during the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time **in your leisure time**?

_____ **days per week**

☐ No walking in leisure time → ***Skip to question 22***

21. How much time did you usually spend on one of those days **walking** in your leisure time?

_____ **hours per day**
_____ **minutes per day**

22. Think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **vigorous** physical activities like aerobics, running, fast bicycling, or fast swimming **in your leisure time**?

_____ **days per week**

☐ No vigorous activity in leisure time → ***Skip to question 24***

LONG LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised October 2002.

23. How much time did you usually spend on one of those days doing **vigorous** physical activities in your leisure time?

_____ **hours per day**
_____ **minutes per day**

24. Again, think about only those physical activities that you did for at least 10 minutes at a time. During the **last 7 days**, on how many days did you do **moderate** physical activities like bicycling at a regular pace, swimming at a regular pace, and doubles tennis **in your leisure time**?

_____ **days per week**

☐ No moderate activity in leisure time → ***Skip to PART 5: TIME SPENT SITTING***

25. How much time did you usually spend on one of those days doing **moderate** physical activities in your leisure time?
_____ **hours per day**
_____ **minutes per day**

PART 5: TIME SPENT SITTING

The last questions are about the time you spend sitting while at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading or sitting or lying down to watch television. Do not include any time spent sitting in a motor vehicle that you have already told me about.

26. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekday**?

_____ **hours per day**
_____ **minutes per day**

27. During the **last 7 days**, how much time did you usually spend **sitting** on a **weekend day**?

_____ **hours per day**
_____ **minutes per day**

This is the end of the questionnaire, thank you for participating.

LONG LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised October 2002.

WHOQOL-BREF

The following questions ask how you feel about your quality of life, health, or other areas of your life. I will read out each question to you, along with the response options. **Please choose the answer that appears most appropriate.** If you are unsure about which response to give to a question, the first response you think of is often the best one.

Please keep in mind your standards, hopes, pleasures and concerns. We ask that you think about your life **in the last four weeks.**

		Very poor	Poor	Neither poor nor good	Good	Very good
1.	How would you rate your quality of life?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
2.	How satisfied are you with your health?	1	2	3	4	5

The following questions ask about **how much** you have experienced certain things in the last four weeks.

		Not at all	A little	A moderate amount	Very much	An extreme amount
3.	To what extent do you feel that physical pain prevents you from doing what you need to do?	5	4	3	2	1
4.	How much do you need any medical treatment to function in your daily life?	5	4	3	2	1
5.	How much do you enjoy life?	1	2	3	4	5
6.	To what extent do you feel your life to be meaningful?	1	2	3	4	5

		Not at all	A little	A moderate amount	Very much	Extremely
7.	How well are you able to concentrate?	1	2	3	4	5
8.	How safe do you feel in your daily life?	1	2	3	4	5
9.	How healthy is your physical environment?	1	2	3	4	5

The following questions ask about how completely you experience or were able to do certain things in the last four weeks.

		Not at all	A little	Moderately	Mostly	Completely
10.	Do you have enough energy for everyday life?	1	2	3	4	5
11.	Are you able to accept your bodily appearance?	1	2	3	4	5
12.	Have you enough money to meet your needs?	1	2	3	4	5
13.	How available to you is the information that you need in your day-to-day life?	1	2	3	4	5
14.	To what extent do you have the opportunity for leisure activities?	1	2	3	4	5

		Very poor	Poor	Neither poor nor good	Good	Very good
15.	How well are you able to get around?	1	2	3	4	5

		Very dissatisfied	Dissatisfied	Neither satisfied nor dissatisfied	Satisfied	Very satisfied
16.	How satisfied are you with your sleep?	1	2	3	4	5
17.	How satisfied are you with your ability to perform your daily living activities?	1	2	3	4	5
18.	How satisfied are you with your capacity for work?	1	2	3	4	5
19.	How satisfied are you with yourself?	1	2	3	4	5

20.	How satisfied are you with your personal relationships?	1	2	3	4	5
21.	How satisfied are you with your sex life?	1	2	3	4	5
22.	How satisfied are you with the support you get from your friends?	1	2	3	4	5
23.	How satisfied are you with the conditions of your living place?	1	2	3	4	5
24.	How satisfied are you with your access to health services?	1	2	3	4	5
25.	How satisfied are you with your transport?	1	2	3	4	5

The following question refers to how often you have felt or experienced certain things in the last four weeks.

		Never	Seldom	Quite often	Very often	Always
26.	How often do you have negative feelings such as blue mood, despair, anxiety, depression?	5	4	3	2	1

Do you have any comments about the assessment?

_____

_____

[The following table should be completed after the interview is finished]

		Equations for computing domain scores	Raw score	Transformed scores*	
				4-20	0-100
27.	**Domain 1**	(6-Q3) + (6-Q4) + Q10 + Q15 + Q16 + Q17 + Q18 ☐ + ☐ + ☐ + ☐ + ☐ + ☐ + ☐	a. =	b:	c:
28.	**Domain 2**	Q5 + Q6 + Q7 + Q11 + Q19 + (6-Q26) ☐ + ☐ + ☐ + ☐ + ☐ + ☐	a. =	b:	c:
29.	**Domain 3**	Q20 + Q21 + Q22 ☐ + ☐ + ☐	a. =	b:	c:
30.	**Domain 4**	Q8 + Q9 + Q12 + Q13 + Q14 + Q23 + Q24 + Q25 ☐ + ☐ + ☐ + ☐ + ☐ + ☐ + ☐ + ☐	a. =	b:	c:

* See Procedures Manual, pages 13-15

DERMATOLOGY LIFE QUALITY INDEX

DLQI

Hospital No: Date:
Name: Score:
Address: Diagnosis:

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	❒ ❒	 Not relevant ❒
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	❒ ❒ ❒	
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 A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒
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 A lot A little Not at all	❒ ❒ ❒ ❒	 Not relevant ❒

Please check you have answered EVERY question. Thank you.

Appendix B: Other Study Documents

11/30/10

CONSENT FORM

Associations between physical activity, disease severity, and quality of life in psoriasis

Introductory:
You are invited to participate in a research study on physical activity and psoriasis. You were selected as a possible participant because you responded to an advertisement for this study. We ask that you read this form and ask any questions you may have before agreeing to be in the study.

This study is being conducted by Patrick Wilson, R.D., L.D., of the School of Kinesiology at the University of Minnesota.

Study Purpose:
You have been asked to take part in a study that aims to determine the physical activity levels of people with psoriasis, which is a common, chronic disorder of the skin. Physical activity is any type of body movement that requires energy. Physical activity involves everyday activities such as walking to work, performing housework, and doing yard work, as well as planned activities such as running, bicycling, and organized sports such as soccer, basketball, etc. In addition, the study will try to find out if physical activity relates to psoriasis severity and quality of life in people with psoriasis.

Study Procedures:
If you decide to take part in this study, you will be asked to fill out five questionnaires. The questionnaires are described below:

- ✓ The self-administered Psoriasis Area and Severity Index (SAPASI). This questionnaire will ask you to judge how much of your body is covered by psoriasis and how severe your symptoms such as skin redness, thickness, and scaling are.
- ✓ The International Physical Activity Questionnaire (IPAQ). This questionnaire will ask about how much physical activity you have done in the past seven days in all areas of your life, including at home, at work, and in your spare time.
- ✓ The World Health Organization Quality of Life questionnaire (WHOQOL-BREF). This questionnaire will ask about your overall health, difficulty in completing day-to-day activities, emotional state, and physical pain. It is intended to measure how you feel about your overall well-being.
- ✓ The Dermatology Life Quality Index (DLQI). This questionnaire also asks about your quality of life, but the questions are more specific to how your skin symptoms affect your quality of life.
- ✓ Demographic Questionnaire. This questionnaire will ask you to report some background information on yourself, including your age, sex, educational level, duration of psoriasis, current psoriasis treatments, smoking history, and drinking history.

These questionnaires will take approximately 25 minutes to complete. After completing these questionnaires, the researcher will take your height, weight, and waist circumference. This will complete your participation in the study.

Risks or Discomforts of Study Participation:
The study has the following risks. Some of the questions asked may make you feel self-conscious about your psoriasis. You may choose not to answer any of the questions presented to you. In addition, there is a risk that someone outside of the principal investigator, Patrick Wilson, could view your study data. However, precautions will be taken to protect the information you provide, and all personal information such as your name and contact information will be removed from the information you provide.

Benefits of this study:
The benefits to study participation include learning about your current level of physical activity and overall quality of life. There is also possible benefit of increased general knowledge for society regarding the relationship between psoriasis and physical activity. No other benefits are anticipated.

Study Costs and Compensation:
There is no compensation for participating in this study. You will be responsible for any costs incurred traveling to the University of Minnesota, such as gas and parking.

Confidentiality:
The records of this study will be kept private. In any publications or presentations, we will not include any information that will make it possible to identify you as a subject. Your record for the study may, however, be reviewed by departments at the University with appropriate regulatory oversight. Any personal information collected will NOT be made part of any personal medical record. To these extents, confidentiality is not absolute.

Voluntary Nature of the Study:
Participation in this study is voluntary. Your decision whether or not to participate in this study will not affect your current or future relations with the University. If you decide to participate, you are free to withdraw at any time without affecting those relationships.

Questions, Rights and Complaints:
The researcher conducting this study is Patrick Wilson. You may ask any questions you have now, or if you have questions later, **you are encouraged to** contact him at 218-969-1917 or email him at wilso733@umn.edu or his advisor, Stacy Ingraham, Ph.D. at 612-626-0067 or ingra013@umn.edu.

If you have any questions or concerns regarding the study and would like to talk to someone other than the researcher(s), you are encouraged to contact the Fairview Research Helpline at telephone number 612-672-7692 or toll free at 866-508-6961. You may also contact this office in writing or in person at University of Minnesota Medical Center, Fairview-Riverside Campus, 2200 Riverside Avenue, Minneapolis, MN 55454.

You will be given a copy of this form to keep for your records.

Consent statement:

By signing this document, you consent to participate in the study Associations between physical activity, disease severity, and quality of life in psoriasis directed by Patrick Wilson, graduate student at the University of Minnesota. I have read the above information. I have asked questions and have received answers. I consent to participate in the study.

_____	_____
Signature of Participant	Signature of Investigator
_____	_____
Typed/printed Name	Typed/printed Name
_____	_____
Date	Date

Psoriasis Study

Graduate student study looking for individuals with psoriasis to participate in a study on exercise and psoriasis severity. The study will involve:

- Filling out a few questionnaires
- Taking a few measurements (height, weight, etc)
- Will take approximately 30 minutes

Contact person: (218) 969-1917 or wilso733@umn.edu

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Appendix C: Additional Physical Activity Data

IPAQ Data Expressed as MET-minutes/week		
Activity Type	*MET-minutes/week*	
	Mean	*SD*
Job walking	836.4	2076.1
Job moderate	255.7	875.3
Job vigorous	539.1	2011.5
Job activity total	1631.2	3489.3
Transportation walking	259.7	455.3
Transportation bicycling	125.2	336.5
Transportation activity total	384.9	675.7
Domestic yard moderate	386.9	593.9
Domestic yard vigorous	286.9	454.1
Domestic inside moderate	530.2	835.9
Domestic activity total	1204.1	1405.8
Leisure walking	403.9	683.3
Leisure moderate	95.7	191.7
Leisure vigorous	457.4	670.7
Leisure activity total	957.0	1055.2
Walking total	1500.1	2496.6
Moderate activity total	1680.7	1717.2
Vigorous activity total	996.5	1996.4

IPAQ Data Expressed as Minutes/week		
Activity Type	*Minutes/week*	
	Mean	*SD*
Job walking	253.4	629.1
Job moderate	63.9	218.8
Job vigorous	67.4	251.4
Job activity total	384.7	805.1
Transportation walking	78.7	138.0
Transportation bicycling	20.9	56.1
Transportation activity total	99.6	170.4
Domestic yard moderate	96.7	148.5
Domestic yard vigorous	52.2	82.6
Domestic inside moderate	176.7	278.7
Domestic activity total	325.7	402.3
Leisure walking	122.4	207.1
Leisure moderate	23.9	47.9
Leisure vigorous	57.2	83.8
Leisure activity total	203.5	249.2