Psoriasis and psoriatic arthritis are inflammatory immune-mediated skin and joint conditions with major impacts on patients' health-related quality of life (HRQOL). Physical manifestations include unsightly, scaly, pruritic plaques and inflamed joints for patients with psoriatic arthritis. These symptoms can severely impair physical functioning and occupational capability and negatively affect psychosocial domains. Consequently, patients often experience feelings of embarrassment, helplessness, and depression. Recent therapies, including the biologics, have been shown to improve not only the physical signs and symptoms of these conditions, but also patients' HRQOL. To accurately assess these improvements, standardized and validated instruments are needed. However, there are currently a limited number of feasible and validated tools available in dermatology for measuring HRQOL and function. Valuable insights can be acquired from the rheumatology field, and refinement of existing outcome measures through a cooperative and consensus building process between dermatologists and rheumatologists will lead to standardization of assessment tools in the years ahead. (J Am Acad Dermatol 2006;54:685-704.)

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Quality-of-life issues in psoriasis and psoriatic arthritis: Outcome measures and therapies from a dermatological perspective

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Seattle, Washington, and Dallas, Texas

Psoriasis and psoriatic arthritis are inflammatory immune-mediated skin and joint conditions with major impacts on patients' health-related quality of life (HRQOL). Physical manifestations include unsightly, scaly, pruritic plaques and inflamed joints for patients with psoriatic arthritis. These symptoms can severely impair physical functioning and occupational capability and negatively affect psychosocial domains. Consequently, patients often experience feelings of embarrassment, helplessness, and depression. Recent therapies, including the biologics, have been shown to improve not only the physical signs and symptoms of these conditions, but also patients' HRQOL. To accurately assess these improvements, standardized and validated instruments are needed. However, there are currently a limited number of feasible and validated tools available in dermatology for measuring HRQOL and function. Valuable insights can be acquired from the rheumatology field, and refinement of existing outcome measures through a cooperative and consensus building process between dermatologists and rheumatologists will lead to standardization of assessment tools in the years ahead. (J Am Acad Dermatol 2006;54:685-704.)

Abbreviations used:
AIMS: Arthritis Impact Measurement Scale
DLQI: Dermatology Life Quality Index
DQOLS: Dermatology Quality of Life Scales
GHQ: General Health Questionnaire
HAQ: Health Assessment Questionnaire
HRQOL: health-related quality of life
KMPI: Koo-Menter Psoriasis Instrument
NHP: Nottingham Health Profile
NPF: National Psoriasis Foundation
OMERACT: Outcome Measures Rheumatoid Arthritis Clinical Trials
PASI: Psoriasis Area and Severity Index
PDI: Psoriasis Disability Index
PLSI: Psoriasis Life Stress Inventory
PQOL-12: psoriasis-specific HRQOL 12-item scale
PsA: psoriatic arthritis
PsAQOL: Psoriatic Arthritis Quality of Life [measure]
RA: rheumatoid arthritis
SF-36: Short-Form-36 Health Survey
SIP: Sickness Impact Profile
SPI: Salford Psoriasis Index
TNF: tumor necrosis factor

psychological burden associated with dermatoses and arthritides, especially psoriasis and PsA.1-6 These studies have reported the stress and disruption in the daily routines of patients, which, in turn, affect their ability to pursue valued life goals.

Psoriasis and its related PsA are inflammatory immune-mediated conditions that have been shown to have major impacts on patients' health-related
quality of life (HRQOL).\textsuperscript{1,4,6-10} Psoriasis is a chronic relapsing skin disorder affecting 2% of the population, presenting as scaly, erythematous plaques.\textsuperscript{11,12} PsA is a spondyloarthropathy with a prevalence reported from 5% to 42% of patients with psoriasis, with potential for significant joint destruction contributing to pain and disability.\textsuperscript{13,14} The overt signs and symptoms of psoriasis and PsA often leave patients with an acute and sometimes distorted perception of their self image as well as a feeling of embarrassment about their appearance. The emotional burden of carrying such a stigma often leads to a significant decline in the patient’s well-being.

In this article, we discuss the impact of psoriasis and PsA on patients’ HRQOL by examining the effects of these conditions on patients’ functional capabilities and on their psychosocial well-being. We also describe some of the currently accepted outcome measures used by dermatologists and rheumatologists to assess quality of life and review recent clinical trials evaluating the effects of psoriatic therapies in the improvement of HRQOL.

**IMPACT OF PSORIASIS AND PSORIATIC ARTHRITIS ON QUALITY OF LIFE**

Measurement of disease activity and impact involves assessment of both physical signs as well as subjective experience. A 75% reduction in the Psoriasis Area and Severity Index (PASI 75) is considered a primary end point in clinical trials of psoriasis.\textsuperscript{15-17} PASI is a calculation based on the parameters of erythema, scaling, and induration in 4 body areas using the rule of 9%.\textsuperscript{18} However, a 50% improvement (PASI 50) has recently been shown to be a valid and clinically meaningful measure.\textsuperscript{19} Although the PASI measures disease severity at the time of assessment, it does not provide any information about the patient’s psychological and mental well-being. In fact, for many diseases like psoriasis and PsA, two patients with similar disease manifestations, such as a similar PASI score, may be affected quite differently by their disease. Therefore quality-of-life measures are as important as physiological or biological measures in evaluating the consequences of a disease. Measuring HRQOL provides a complementary assessment of the patient’s overall well-being because it defines the functional effect of an illness and its therapy based on the patient’s own perception. In general, HRQOL encompasses the physical and psychosocial (psychological, social, and vocational) impairment related to the disease, as well as the therapeutic regimens associated with its treatment.\textsuperscript{20} Recognizing the tremendous impact that psoriasis and PsA have on daily activities are important for understanding the significant challenges patients have to cope with in living with these disfiguring and disabling skin and joint disorders.

**Physical impact**

Visible manifestations of psoriasis take the form of circumscribed, thickened, scaly plaques that are often pruritic.\textsuperscript{11,12} Lesions may be localized to individual areas such as the scalp, elbows, knees, and buttocks or involve the total body surface area as in erythrodermic psoriasis.\textsuperscript{11,12} The extent and duration of the symptoms may vary according to the severity of the skin disease, ranging from itching, irritation, and redness to physical pain, skin soreness, bleeding from psoriatic lesions, fatigue, and insomnia.

In addition to their skin lesions, patients with PsA also are faced with the painful and potentially disabling effects of arthritis. The joint inflammation in PsA frequently involve the digits (dactylitis), the spine and back (spondylitis), and the site of insertion between the tendons and ligaments (enthesitis).\textsuperscript{14} Skin lesions usually precede arthritis by 5 to 10 years in most patients with PsA.\textsuperscript{21} Involved joints are warm and swollen, resulting in pain and discomfort and limiting the patient’s mobility. Over time, cartilage and bone erosion in PsA can lead to significant deformities and permanent disability.

The cumulative effects of the disease, in either the skin alone or the skin and joints, all contribute to decrements in patients’ physical functioning status. Physical functioning includes the patient’s mobility, daily activities, energy/vitality, and sleeping habits.\textsuperscript{22} For many patients, activities such as walking, climbing stairs, and routine occupational duties (eg, typing or lifting) are significantly impaired.\textsuperscript{6,22} Rapp et al\textsuperscript{9} showed that patients with psoriasis had significant decrements in their physical functioning capacity that was comparable to those of patients with other major medical conditions, including cancer, arthritis, hypertension, heart disease, diabetes, and depression. In a large survey sponsored by the National Psoriasis Foundation (NPF) in the United States, Krueger et al\textsuperscript{5} reported that elderly patients (≥55 years old) had the greatest physical impairments and were more likely to report difficulties in daily living activities such as using their hands (19%) or walking (14%). Limitations in performing these activities may be exacerbated in patients with PsA because of mobility issues associated with the arthropathy, with more than 60% of elderly patients with PsA reporting difficulties in using their hands, standing for long periods, and walking.\textsuperscript{6} Psoriasis may also compromise the patient’s ability to sleep well, which, in turn, adversely affects their energy level and the ability to perform their jobs.\textsuperscript{6,22} Although patients
with PsA have reported higher levels of energy than patients with rheumatoid arthritis (RA), they nevertheless experience lesser physical health compared with the general population. \(^4\) Furthermore, compared with RA patients, patients with PsA reported more bodily pain.

Psoriatic patients frequently have to alter their daily routines and generally avoid social activities. In the NPF survey, 26% claimed that their disease forced them to alter or stop their normal daily activities and 40% reported difficulties with their choice of clothing. \(^6,23\) In a large European survey conducted by the European Federation of Psoriasis Patients Organisations, a significant proportion of patients also reported having difficulties choosing their clothes (46%), and changing their clothes (38%), bathing (37%), and engaging in sport activities (20%). \(^*,**\)

Psoriasis also adversely affects patients’ occupational capability, which can lead to significant financial difficulty. \(^6\) Patients have reported discrimination at work and job disruptions because of the time needed for medical attention or because of physical limitations imposed by their disease. In one study, as many as 59% of patients required time off from work during the preceding year. \(^1\) Those with severe forms of PsA may also find that they can no longer physically perform their usual duties, such as lifting boxes or filing documents as part of their daily routines, and are either forced into early retirement or unemployment. The financial burden is often substantial and includes the cost of care, the time needed for medical care, lost wages from time off, and unemployment due to disability. \(^2,24\) The impact of psoriasis on financial quality of life is even greater for patients with lower family income. \(^6\) Overall, 31% of patients in the NPF survey reported suffering financial difficulty. Among those earning less than $30,000 a year, 42% faced financial difficulties and lived in fear of losing their jobs. \(^6\)

**Psychosocial impact**

The burden of coping with the physical problems associated with psoriasis and PsA inevitably affects psychosocial domains. Pruritus, in particular, is associated with distressing symptoms and depression. \(^25\) Because psoriasis usually begins early in life (60% before the age of 30 and 14% before the age of 10), \(^26\) changes of physical appearance and any accompanying psychosocial effects are an enduring hardship.

The impacts of dermatological diseases on patients’ lives are substantial and have been consistently underestimated. Psoriasis and PsA are associated with significant psychosocial morbidity and a reduction in HRQOL. Of the patients who responded to the extensive 2001 NPF survey, 79% believed psoriasis had a negative impact on their lives. \(^6\) This finding was almost identical to a more recent NPF survey, which found that 77% of patients considered psoriasis to be a moderate to-large problem in their lives. \(^23\) Similar responses were found among Europeans in the European Federation of Psoriasis Patients Organisations survey, in which 60% of patients reported that their psoriasis was a problem or a significant problem. \(^*,**\) As discussed previously, patients experience feelings of embarrassment, helplessness, and frustration about their disease. \(^27\) Unresolved emotional problems can often deteriorate into more intense feelings of anger, anxiety, and depression that may lead to increased alcohol use and other behavioral changes. A majority of patients (54%) in the 2001 NPF survey reported feeling depressed and experiencing significant life disruptions and social withdrawal as a result of their disease. \(^6\) Additionally, Gupta and Gupta \(^28\) found that many patients had a death wish (9.7%) and suicidal ideation (5.5%), especially prevalent in younger people and a considerable increase over that found in the nonpsoriatic population.

In addition, patients with psoriasis generally have low self-esteem. Thus 81% have reported feeling embarrassment and shame, whereas 75% reported feeling physically unattractive and/or sexually undesirable. \(^5,22\) Afflicted patients are conscious about the clothes they wear and the social events they attend. Many report limitations with skin exposing social activities, such as communal swimming, sports activities, and sunbathing. \(^6,22\) These limitations may not necessarily be of the patient’s making, considering that 40% have reported experiencing problems with receiving equal service or treatment in various service establishments, \(^6\) and 19% have reported experiencing instances of gross social rejection, such as being asked to leave a place because of their disease. \(^29\) Social contacts and intimate relationships are also negatively affected, with a significant decrease of sexual functioning observed for many patients. \(^6,22\)

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\(*Salonen SH on behalf of the EUROPSO Patient Survey Study Group. Large-scale European Survey of Quality of Life in Patients with Psoriasis: Second-phase results on quality of life and treatment reported by 7,575 members of European psoriasis patient associations. The EUROPSO Psoriasis Patient Study. Presented at the 10th International Psoriasis Symposium, June 10-13, 2004, Toronto, Canada.\)

\(^1\)Salonen SH on behalf of the EUROPSO Patient Survey Study Group. The EUROPSO psoriasis patient study: Treatment history and satisfaction reported by 17,990 members of European psoriasis patient associations. The EUROPSO Psoriasis Patient Study. Presented at the 1st European Academy of Dermatology and Venereology Spring Symposium, Feb 27-March 1, 2003, Malta.
Table I. Commonly used quality-of-life measures in rheumatology

<table>
<thead>
<tr>
<th>Psychosocial dimensions</th>
<th>Instruments</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Beck Depression Inventory</td>
<td>Beck et al (1961)</td>
</tr>
<tr>
<td></td>
<td>GHQ</td>
<td>Chanderana et al (1987)</td>
</tr>
<tr>
<td></td>
<td>SF-36</td>
<td>Ware, Snow, and Kosinski (2000)</td>
</tr>
<tr>
<td></td>
<td>Likert Scale</td>
<td>Fries et al (1982)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>FACIT</td>
<td>Cella et al (2002)</td>
</tr>
<tr>
<td></td>
<td>MAF</td>
<td>Belza (1995)</td>
</tr>
<tr>
<td></td>
<td>NHP</td>
<td>McEwen (1993)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>GHQ</td>
<td>Chanderana et al (1987)</td>
</tr>
</tbody>
</table>

AIMS, Arthritis Impact Measurement Scale; FACIT, Functional Assessment of Chronic Illness Therapy; FSS, Fatigue Severity Scale; GHQ, General Health Questionnaire; HAQ, Health Assessment Questionnaire; MAF, Multidimensional Assessment Fatigue Scale; MFI, Multidimensional Fatigue Inventory; NHP, Nottingham Health Profile; SF-36, Medical Outcomes Study Short Form-36; VAS, Visual Analogue Scale.

Patients with psoriasis and PsA rarely experience death directly because of their disease or its treatment. Even in reported cases of death of patients due to psoriasis, the primary cause of mortality is related predominantly to its therapy (eg, methotrexate [MTX] and methoxypsoralen plus ultraviolet A therapy). Although deaths directly related to PsA are rare, in one center patients with PsA had premature mortality compared with the general public. Wong et al observed that of the 428 patients from an outpatient clinic, 53 died of causes ranging from diseases of circulatory or respiratory systems, malignant neoplasms, and fatal injuries and/or poisoning. This was considered to be 67% higher than the background mortality rate in that region. Although these deaths were not directly linked to PsA, the higher incidence raises the possibility of comorbidity that could be affected by more effective and timely treatment.

HRQOL is a relatively new area of research focus in psoriasis because of a growing awareness among dermatologists that physical manifestations such as redness, scaling, and induration represent only a portion of the impairment and the potential dramatic impact of therapy on HRQOL. There are currently a limited number of feasible and validated tools available to measure HRQOL and function. Based on the relatively large body of literature on HRQOL and assessment tools that have been developed for rheumatic diseases over the years, the rheumatology field is able to provide some valuable insights.

LESSONS LEARNED FROM RHEUMATOLOGY

Several rheumatology studies have shown that the mechanisms underlying the pathogenesis of psoriasis and other rheumatic diseases, including adult and juvenile RA, PsA, and ankylosing spondylitis are mediated by a similar network of proinflammatory cytokines (eg, tumor necrosis factor-α [TNF-α] and interleukin 1) and cellular components (eg, T cells, fibroblasts, and macrophages). In many cases, therapeutic approaches that are successful in treating RA and other musculoskeletal diseases have been demonstrated to be equally effective in alleviating the signs and symptoms of psoriasis and PsA, as well as in improving patients’ HRQOL.

As a result of these therapeutic advances, measurements of physiological and psychosocial factors in rheumatic diseases have been continuously refined over the years to provide more accurate and reliable tools. The development and validation of these instruments have been facilitated by the concerted efforts of rheumatologists to standardize outcome measures that truly reflect specific areas of a patient’s health that are being evaluated. These efforts are focused in OMERACT (Outcome Measures in Rheumatoid Arthritis Clinical Trials), an international initiative that strives to improve outcome measurement through a data-driven, iterative consensus process, based on the collaboration of investors, industry, and Food and Drug Administration representatives. The biostatistical quality of outcome measures used in trials is critically assessed and judged by the standard of the OMERACT filter, that is, truth (does the instrument have face, content, construct, and criterion validity?), discrimination (is the measure reliable and sensitive enough to discriminate between situations that are of interest?), and feasibility (can the measure be applied easily, given constraints of time, money, and interpretability?).
and pain. A modification of the HAQ, called the HAQ-S, has been developed for spondyloarthropathies and tested in patients with PsA. Although the HAQ-S measures physical disability, it only incorporates aspects of disability associated with the joints, but not the skin. In addition, the HAQ-S does not confer any advantage over the original HAQ when tested in patients with PsA, which may limit its usefulness. Other measures of disability include the Arthritis Impact Measurement Scale (AIMS) and AIMS-2 for the assessment of PsA,45,46 and the Bath Ankylosing Spondylitis Functional Index and the Bath Ankylosing Spondylitis Disease Activity Index for the assessment of ankylosing spondylitis.47,48 Generic instruments, such as the Medical Outcome Study Short Form-36 (SF-36) and the EUROQOL (EQ-5D), are also valuable tools for evaluating physical disability and can be utilized in studies of all rheumatic and dermatologic diseases.49-51

In addition to disability, physical parameters such as pain and fatigue are also measurable features of RA and spondyloarthropathies. Pain is commonly assessed using a visual analogue scale or the Likert scale, both of which are included as subscales in many instruments, including the HAQ and the SF-36.52,53 Disease-related fatigue can be evaluated by using a variety of instruments including the following: the Functional Assessment of Chronic Illness Therapy,54 the Krupp Fatigue Severity Scale,55 the Multidimensional Assessment Fatigue scale,56 the Multidimensional Fatigue Inventory,57 or the Nottingham Health Profile (NHP).58

Assessing psychosocial well-being in rheumatic and dermatologic conditions is an especially important dimension to measure because of their impact on emotional and psychological well-being. In clinical trials, much of the emphasis has been on depression and anxiety. Measures like the Beck Depression Inventory59 or more generic instruments, such as the General Health Questionnaire (GHQ) and the SF-36, are self-administered questionnaires that include depression and/or anxiety subscales.50,60 Other psychosocial variables include social support, coping skills, health cognition, spirituality, and positive mood, all of which require specialized instruments for measurement.53,61 The World Health Organization and OMERACT recently introduced the concept of “participation in life” as another important facet of HRQOL.62 “Participation” is defined as a patient’s social functioning status or real-life performance and involvement in community and recreational activities. It can also be described as the patient’s willingness and enthusiasm to pursue valued life goals despite the limitations imposed by the disease and other social and environmental factors. Although there are currently no measures for assessing “participation,” these instruments are in development.

The large number of outcome measures utilized in the study of rheumatic diseases underscores the complexity involved in the assessment of HRQOL. Generally, it has been recommended that clinical trials include one generic measure of health status (eg, SF-36) and one instrument specific either to a disease (eg, PsA or RA), to a problem (eg, pain), or to a patient population (eg, child vs adult).53,64 Disease-specific instruments such as the Rheumatoid Arthritis Quality of Life measure, the Ankylosing Spondylitis Quality of Life measure, and the Psoriatic Arthritis Quality of Life measure have all purported to assess very specific aspects of quality of life unique to their respective disease.65-67 In addition to specificity, disease-specific instruments have been shown to have increased sensitivity and responsiveness to small but clinically important changes, compared with generic instruments.20,68 However, one of the advantages of generic instruments is that they provide additional information about comorbid conditions or treatment side-effects that are not easily captured by specific instruments. Thus generic and specific instruments are complementary measures that, when combined, provide a comprehensive assessment of the patient’s overall well-being.

In dermatology, evaluating quality of life in patients with psoriasis and PsA requires similarly validated and standardized instruments. Forums that are modeled after OMERACT would provide an appropriate setting for academic and practicing dermatologists to engage in thoughtful discussions and critiques of the kinds of outcome measures that would be most valuable to the dermatology world. An example of such a forum is the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis. Formed in 2003, this international consortium of rheumatologists and dermatologists is focused on a variety of tasks, ranging from establishing clinical registries to development of treatment guidelines to standardization and validation of outcome measures for clinical trials in psoriasis and PsA. This includes evaluation and refinement of measures of quality of life, function and participation, which will in turn be further ratified by OMERACT. A newly formed international psoriasis consortium, the International Psoriasis Council, will be a similar forum specifically focused on psoriasis issues. Ideally, any instruments that are adopted should achieve test retest reliability, internal consistency, and face and construct validity, comparable to the OMERACT filter. As with RA and other rheumatic diseases, utilization of multiple instruments may be warranted.
in psoriasis to capture the various dimensions of HRQOL. For PsA, the choice of instruments will also depend on which areas—skin or joints—the patient considers of higher importance. For instance, patients experiencing severe joint damage due to PsA may be less concerned about their appearance if they are faced with the possibility of being permanently handicapped. Age is another factor, with younger patients more likely to be concerned about their appearance (skin-focused), whereas elderly patients are more likely to worry about physical disability (joint-focused).6 Dermatologists and rheumatologists frequently have different views that are inevitably biased toward their areas of expertise. To reconcile these differences, efforts are under way to develop HRQOL tools that have dual purposes for assessing the impact of both psoriasis and arthritis in PsA patients.66,69

MEASURES OF QUALITY OF LIFE IN PSORIASIS AND PSORIATIC ARTHRITIS

Over the past few years, assessments of HRQOL in patients with skin conditions have become more common in clinical trials. The increased attention to HRQOL is a consequence of a greater understanding within the dermatology community that more comprehensive outcome measures can lead to better treatment strategies by providing valuable information that assists clinicians and patients. To accurately assess HRQOL, precise and reliable psychometric instruments are needed. Currently, there is no consensus as to which measures provide the most benefit to dermatologists. In the following sections, we describe some of the widely used generic, dermatology-specific, and psoriasis-specific instruments and discuss their merits.

Generic instruments

In the past several years, several researchers have applied existing patient-reported instruments, such as the HAQ and the SF-36, to clinical trials of psoriasis and PsA.39,70-75.* Although these tools have been somewhat successful in capturing the functional impairment associated with joint damage in PsA, their clinical utility in skin-based assessments of psoriatic patients is limited.

The HAQ43 has been used extensively for measuring disability in patients with RA, ankylosing spondylitis, and PsA (Table II). A modified HAQ for spondyloarthopathies (HAQ-S), and a psoriasis-specific HAQ (HAQ-SK), were developed to increase specificity and sensitivity, but these instruments did not enhance the health assessment capabilities of the original HAQ.44,76,77 Both the HAQ and the HAQ-S scores were shown to correlate with several clinical measures of functional disability in patients with PsA.78 However, these scores correlated poorly with all measures of disease severity (eg, PASI scores) and disease activity.76 The HAQ-SK, despite including more skin-focused questions, also did not correlate well with the PASI score and was not very responsive to articular changes.77 These findings suggest that the HAQ and its derivatives may not be appropriate for the majority of psoriasis patients because it places too much weight on physical symptoms (impairment) and/or functioning (activity or disability). Although the HAQ may be applicable to studying joint-related impairments in PsA, it does not provide adequate assessments of skin-related discomfort or psychosocial problems. This problem is most obvious among patients with psoriasis who continue to experience low quality of life despite the absence of any skin lesions and physical disability during remission.

The SF-36, a generic health assessment questionnaire, has been used in many clinical trials to study the impact of several different types of chronic diseases, including several rheumatic disorders. It assesses 8 domains of health status: physical functioning, pain, vitality, social functioning, psychological functioning, general health perceptions, and role limitations due to physical and emotional problems (Table II).50 As a measure of both the physical and mental impact of a disease, the SF-36 has the ability to assess a broad spectrum of dimensions in HRQOL and can be used in comparative analyses of various patient groups across multiple studies.

Several clinical trials of PsA have utilized the SF-36 as an outcome measure for HRQOL.74,75,1 Husted et al77 demonstrated that the SF-36 was equally or more responsive to short-term changes in perceived health and inflammatory disease activity than either the HAQ or the AIMS-2. However, the SF-36 correlates only moderately with clinical indicators of function, pain, and arthritis activity in patients with PsA.78 One of the limitations of the SF-36 is that it emphasizes impairment and physical disability and does not give equal weight to important issues relevant to psoriasis such as stigmatization and embarrassment.79 Clinical trials of patients with

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Table II. Instruments for measuring quality of life in psoriasis and/or psoriatic arthritis

<table>
<thead>
<tr>
<th>Instrument</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>Generic</strong></td>
<td></td>
</tr>
<tr>
<td>HAQ and variants</td>
<td>- The full HAQ is based on 5 dimensions: disability, pain and discomfort, adverse treatment effects, dollar costs of treatment, and death</td>
</tr>
<tr>
<td></td>
<td>- The abbreviated form focuses on 2 dimensions of health status: physical disability (20 questions in 8 subscales scored on a scale of 0-3) and pain (1 question scored on a horizontal visual analogue scale of 0-100)</td>
</tr>
<tr>
<td>SF-36</td>
<td>- 36-item generic measure that consists of 8 scales of health status: physical function, role limitations due to physical problems, body pain, vitality/energy, social functioning, general health, mental health, and role limitations due to emotional problems</td>
</tr>
<tr>
<td></td>
<td>- Can be aggregated into 2 summary scores: Physical Component Summary and Mental Component Summary</td>
</tr>
<tr>
<td></td>
<td>- Scoring is on a 100-point scale, with a change of 5 points considered clinically significant</td>
</tr>
<tr>
<td><strong>Dermatology-specific</strong></td>
<td></td>
</tr>
<tr>
<td>DLQI</td>
<td>- 10-item instrument measures symptoms (1 item), feelings (1 item), daily activities (2 items), leisure (2 items), work/school (1 item), relationship (2 items), and treatment (1 item), with each item graded on a Likert scale of 0-3 for a maximum score of 30</td>
</tr>
<tr>
<td></td>
<td>- Patients answer questions with regard to previous 7 days</td>
</tr>
<tr>
<td>DQOLS</td>
<td>- 41 items consisting of psychosocial subscales (embarrassment [5 items], despair [5 items], irritability [3 items], distress [4 items]), physical activities subscales (everyday [6 items], summer [3 items], social [2 items], sexual [1 item]), and symptoms (12 items)</td>
</tr>
<tr>
<td></td>
<td>- Each item rated on a Likert scale of 0-4 for a maximum score of 100</td>
</tr>
<tr>
<td><strong>Psoriasis-specific</strong></td>
<td></td>
</tr>
<tr>
<td>KMPI</td>
<td>- 12-item instrument derived from the 41-item Psoriasis QOL questionnaire, and graded on a scale of 0-10 for a maximum score of 120</td>
</tr>
<tr>
<td></td>
<td>- Based on assessment of previous month</td>
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<tr>
<td></td>
<td>- Total score of 50 or higher indicative of patients who should be considered for systemic therapy</td>
</tr>
<tr>
<td></td>
<td>- The information characterizes disease status in terms of its impact on quality of life, body surface area affected, the presence of joint involvement, and certain severe forms of psoriasis, and whether phototherapy is an option.</td>
</tr>
<tr>
<td>PDI</td>
<td>- 15-item version derived from a 10-item instrument designed to quantify functional lifestyle disability 4 weeks before and 4 weeks after treatment</td>
</tr>
<tr>
<td></td>
<td>- Covers 5 areas: daily activities (5 items), work or school (3 items), personal relationships (2 items), leisure (4 items), and treatment (1 item)</td>
</tr>
<tr>
<td></td>
<td>- Scored on a visual analogue scale of 1-7 with a maximum score of 105, or a graded 4-point tick-box system</td>
</tr>
<tr>
<td>PLSI</td>
<td>- 15-item instrument based on an original 41-item questionnaire designed to provide an index of psoriasis-related stress</td>
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<tr>
<td></td>
<td>- Covers stress associated with cosmetic disfigurement/social stigma (11 items) and stress associated with symptoms of the disease and/or inconvenience of treatment (4 items)</td>
</tr>
<tr>
<td></td>
<td>- Each item graded on a scale of 0-3, for a maximum score of 45, based on assessment of previous month</td>
</tr>
<tr>
<td>SPI</td>
<td>- Derived from combining a score of current severity of psoriasis based on the PASI (signs), a score indicating psychological disability, and a score based on historical information (interventions)</td>
</tr>
<tr>
<td></td>
<td>- The SPI transforms the PASI into a number from 0-10, assigns a score of 0-10 to psychological disability based on the visual analogue scale, and a score of 1-5 for historical information.</td>
</tr>
</tbody>
</table>

*Other widely used generic questionnaires: General Health Questionnaire; Nottingham Health Profile, Sickness Impact Profile, Satisfaction with Life Scale.*
psoriasis have found that the SF-36 does not have the discriminative capacity to distinguish between treatment groups and placebo.\textsuperscript{70,71} 

Despite these limitations, non–disease-specific instruments are valuable because they provide supplementary assessments that would not otherwise be available to dermatologists, particularly during evaluations of patients with PsA. In addition to the HAQ and the SF-36, other general outcome measures that have been tested in psoriasis studies include the AIMS,\textsuperscript{85,86} the NHP,\textsuperscript{80} the GHQ,\textsuperscript{81} and the Sickness Impact Profile (SIP).\textsuperscript{82} Further studies are needed to ascertain which of these instruments are best suited for assessments of skin-based HRQOL in these diseases.

**Dermatology-specific instruments**

The **Dermatology Life Quality Index**. The Dermatology Life Quality Index (DLQI) is a 10-item instrument that was developed as a measure of disability based on the responses of 120 dermatology outpatients.\textsuperscript{83} It is used in a wide range of dermatological conditions and across a wide range of disease severity as a quality of life instrument. The 10 items of the questionnaire focus on a variety of health dimensions, including symptoms, feelings, daily activities, leisure, work/school, relationships, and treatment (Table II). Patients answer questions on a 0-3 Likert scale based on their experience during the previous 7 days. The scores are then tabulated and expressed as a number from 0 to 30 or, alternatively, as a percentage of the maximum score, with higher values indicative of poorer outcomes.

The DLQI has been the most utilized and validated instrument of HRQOL in psoriasis. It is short, practical, and applicable to many dermatological disorders. Finlay and Khan\textsuperscript{83} showed that DLQI scores for patients with psoriasis, atopic eczema, generalized pruritus, viral warts, and acne were all significantly higher than those for control patients, thus demonstrating discriminant and construct validity. The DLQI was found to have high reliability and internal consistency.\textsuperscript{83,84} Additionally, several studies have shown that the DLQI is sensitive and responsive to clinical changes in quality of life following various therapies (Table III).\textsuperscript{10,16,70,71,73,85-88} A strong correlation between the DLQI and the Psoriasis Disability Index (PDI) has also been demonstrated.\textsuperscript{89} However, the correlation was much lower when compared with measures of disease severity, especially among those with mild to moderate psoriasis.\textsuperscript{83}

The **Dermatology Quality of Life Scale**. The Dermatology Quality of Life Scale (DQOLS) is a 41-item instrument that focuses primarily on areas of psychosocial well-being and was designed to complement the DLQI.\textsuperscript{80} It was derived from a study of 50 dermatology outpatients and includes subscales on psychosocial health, physical activities, and symptoms (Table II). Each item is rated on a 0-4 Likert scale based on the previous 4 weeks. The scores are then standardized to a 100 scale, with the maximum score representing the worst outcome.

The validity of the DQOLS has been tested against the NHP in a group of dermatology patients in the United Kingdom, where it was shown to have higher sensitivity to detect differences between patients with psoriasis versus those with acne.\textsuperscript{80} Sensitivity has also been demonstrated in a few clinical trials, with the DQOLS responsive to improvement in HRQOL after psoriatic treatments (Table III).\textsuperscript{70,71,73} This instrument has high internal consistency and test-retest reliability.\textsuperscript{80} However, one of the main criticisms of the DQOLS is that it is too long and unwieldy to be practical for use in routine clinical practice and could benefit by eliminating redundant questions. Furthermore, it may not adequately capture the impact of PsA.

**Psoriasis-specific instruments**

The **Koo-Menter Psoriasis Instrument**. The Koo-Menter Psoriasis Instrument (KMPI) was originally designed to offer dermatologists a simple and practical assessment tool for quickly and easily identifying patients with psoriasis who may be candidates for systemic therapy (Table II).\textsuperscript{90,91} It is
Table III. Quality-of-life outcomes in recent clinical trials involving patients with either psoriasis or psoriatic arthritis

<table>
<thead>
<tr>
<th>Study</th>
<th>Agents</th>
<th>Patient population</th>
<th>QOL instrument</th>
<th>Treatment outcomes</th>
</tr>
</thead>
</table>
| Koo et al* (2004) | Oral tazarotene | 690 pts with moderate to severe psoriasis | KMPI (also known as PQOL-12) | • At baseline, mean PQOL-12 scores for patients on tazarotene and placebo were 5.39 and 5.43, respectively  
• At wk 12, mean changes in PQOL-12 score for the tazarotene and placebo groups were −1.63 and −0.84, respectively (P < .0001)  
• Mean baseline DLQI scores were 9.1 for placebo control and 8.8 for the leflunomide group  
• At 24 wk, mean change in DLQI scores were significantly higher in leflunomide group (−1.9) compared with placebo (−0.2) (P < .0173)  
• Mean baseline HAQ scores were 1.14 for placebo control and 1.08 for leflunomide group  
• At 24 wk, mean change in HAQ scores were significantly greater in leflunomide group (−0.19) compared with placebo (−0.05) (P < .0267)  
• Mean baseline DLQI for the alefacept group was 11.58 compared with 10.75 for the placebo group.  
• Continuous treatment with alefacept 7.5 mg IV once weekly significantly reduced mean DLQI scores compared with placebo (−4.4 vs −1.8 points, respectively) at 2 wk after last dose (P < .001).  
• At 12 weeks after the last dose:  
  • Mean DLQI reduction for alefacept treatment was −3.4 compared with −1.4 for placebo (P < .001)  
  • Mean change in DQOLS Symptoms scale was significantly greater in patients receiving alefacept compared with placebo (−18.2 vs −11.1, respectively).  
  • Mean changes in SF-36 scores were not significant between the treatment groups.  
  • Efalizumab-treated (1 mg/kg/wk) pts had significantly greater mean improvement from baseline in DLQI score than placebo-treated pts (5.6 vs 1.9 points; P < .001) at wk 12  
  • 51%-61% of efalizumab-treated pts were categorized as “better” on each DLQI scale, compared with 23%-29% of placebo-treated pts  
  • Mean percent improvement from baseline in DLQI score was 46% in the efalizumab group and 15% in the placebo group at wk 12  
  • Mean baseline DLQI scores were 11.3, 12.7, 12.2, and 12.8 for 50-mg BIW etanercept, 25-mg BIW etanercept, the 25-mg QW etanercept, and placebo groups  
  • At wk 12, DLQI response rates were 71% for 50-mg BIW, 64% for 25-mg BIW, and 55% for 25-mg QW groups; all statistically significantly (P < .001) superior to placebo (30%)  

Feldman et al§ (2004) and Krueger et alⅡ (2004) | Etanercept | 652 pts with moderate to severe psoriasis | DLQI | • Mean baseline DLQI scores were 11.3, 12.7, 12.2, and 12.8 for 50-mg BIW etanercept, 25-mg BIW etanercept, the 25-mg QW etanercept, and placebo groups  
• At wk 12, DLQI response rates were 71% for 50-mg BIW, 64% for 25-mg BIW, and 55% for 25-mg QW groups; all statistically significantly (P < .001) superior to placebo (30%)  

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### Table III. Cont’d

<table>
<thead>
<tr>
<th>Study</th>
<th>Agents</th>
<th>Patient population</th>
<th>QOL instrument</th>
<th>Treatment outcomes</th>
</tr>
</thead>
</table>
| Krueger et al\(^{5}\) (2004) | Etanercept | 583 pts with stable, moderate to severe psoriasis | DLQI, SF-36 | • Using more stringent “not at all affected by their psoriasis” responder definition, pts on all but the 25-mg QW dose had clinically meaningful DLQI response (24% for 50-mg BIW, 12% for 25-mg BIW, 6% for 25-mg QW, and 2% for placebo groups)  
• In open-label phase (etanercept 25 mg BIW), mean percent improvements in DLQI were 39% at wk 24, 51% at wk 36, 53% at wk 48, and 54% at wk 60  
• Mean baseline DLQI scores were 11.43, 11.49, and 12.15 for the 50-mg BIW etanercept group, 25-mg BIW etanercept group, and placebo group, respectively  
• At wk 2, relative to patients on placebo, patients on etanercept had achieved statistically significantly \((P < .001)\) greater improvement in DLQI total score  
• Scores increased at each assessment; by wk 12, mean percent improvement in DLQI was 70% for 50-mg etanercept BIW, 65% for 25-mg BIW etanercept, and 6% for placebo groups \((P < .002)\)  
• Improvements in both physical and mental summary scores of the SF-36 were also significantly higher \((P < .01)\) for the etanercept groups at wk 12  
• Mean baseline HAQ was 1.1 for both etanercept and placebo groups  
• Mean improvement in HAQ score was 0.6 unit (54%) at wk 24 in the 25-mg BIW etanercept group and 0.1 unit (6%) in the placebo group \((P < .0001)\)  
• At wk 24, a 0.5-unit improvement in HAQ was seen in 50% of etanercept pts compared with 14% of placebo pts \((P < .0001)\)  
• Mean baseline SF-36 Physical Component Summary scores were 36 units for both groups  
• Improvement in SF-36 Physical Component Summary score was 9.3 units at 24 wk in the etanercept group and 0.7 unit in the placebo group \((P < .0001)\); improvement was sustained for 72 wk  
• Mean change in Vitality SF-36 scores from baseline was 14.6 at wk 24 and 59.5 at wk 72  
• Mean improvement in Feeling Thermometer scores from baseline was 14.3 units in the etanercept group and 2.1 units in the placebo group at wk 24 \((P < .0001)\)  
• Mean baseline DLQI scores were 11.3, 12.7, and 12.2 for the 50-mg BIW, 25-mg BIW, and 25-mg QW etanercept groups, respectively, compared with 12.8 for placebo |
<p>| Mease et al(^{75}) (2004), Mease et al(^{74}) (2003), and Wanke et al(^{7}) (2002) | Etanercept | 205 pts with PsA | HAQ, SF-36, EuroQoL Feeling Thermometer |  |
| Leonardi et al(^{16}) (2004) | Etanercept | 672 pts with stable, moderate to severe psoriasis | DLQI |  |</p>
<table>
<thead>
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<th>Study</th>
<th>Agents</th>
<th>Patient population</th>
<th>QOL instrument</th>
<th>Treatment outcomes</th>
</tr>
</thead>
</table>
| Feldman et al** (2004) | Infliximab | 249 pts with extensive or severe psoriasis | DLQI | • Mean percentage improvements from baseline in DLQI scores were significantly greater in all etanercept groups compared with placebo at wk 12: 61% for 50-mg BIW group, 51% for 25-mg BIW group, 47% for 25-mg QW group, and 11% for placebo group ($P < .001$)  
• Median percent change from baseline in DLQI at wk 10 was 84%, 91%, and 0% for the 3-mg/kg infliximab group, 5-mg/kg infliximab group, and placebo group, respectively ($P < .001$)  
• Mean baseline DLQI scores were 12, 11, and 14 for the 5-mg/kg infliximab group, 3-mg/kg infliximab group, and placebo group, respectively  
• Median change from baseline in DLQI at wk 10 was $-8.0$, $-10.0$, and 0.0 for the 3-mg/kg infliximab group, 5-mg/kg infliximab group, and placebo group, respectively ($P < .001$)  
• 33% of pts in the 3-mg/kg group and 40% of patients in the 5-mg/kg group had a DLQI score of 0 at wk 10, compared with 0% in the placebo group ($P < .001$)  
• The domains evaluating quality of life, including the HAQ, the SF-36, Fatigue Severity Scale, patient visual analogue scale for skin severity, stiffness, and pain did not show statistically significant improvement at wks 14, 30, or 54  
| Feletar et al†† (2004) | Infliximab | 16 pts with PsA | HAQ, SF-36 |  
| Wallace et al††† (2004) | Adalimumab | 148 pts with moderate to severe plaque psoriasis | DLQI | • Pts receiving 40 mg adalimumab EOW and 40 mg adalimumab QW had significantly better mean DLQI scores at wk 12 than placebo-treated patients (2.8 EOW and 2.0 weekly vs 10.7 for placebo; $P < .001$)  
• Mean DLQI change from baseline to week 12 was also significant ($-10.8$ EOW, $-11.5$ weekly vs $-1.3$ placebo; $P < .001$)  
• No significant differences observed in QOL between patients treated with MTX (15 mg/wk) or those treated with CsA (3 mg/kg/d)  
• Mean physical and mental component scores were comparable for the MTX group (52 and 51, respectively) and for the CsA group (53 and 51, respectively) after 16 wk of treatment  
• SF-36 at baseline generally did not indicate impairment in any group, and there were little observed changes in SF-36 scores during therapy  

**Continued**
Table III. Cont’d

<table>
<thead>
<tr>
<th>Study</th>
<th>Agents</th>
<th>Patient population</th>
<th>QOL instrument</th>
<th>Treatment outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Finlay et al 73 (2003)</td>
<td>Alefacept</td>
<td>507 pts with chronic plaque psoriasis</td>
<td>DLQI, DQOLS, SF-36, GHQ</td>
<td>Mean baseline DLQI scores were 9.0, 8.6, and 9.8 for the 0.075-mg/kg alefacept, 0.025-mg/kg alefacept, and placebo groups. At 12 wk after the last dose: Mean change in DLQI Overall scale [% improvement] were significantly greater in patients receiving 0.025- and 0.075-mg/kg alefacept compared with placebo (−4.0 [47%], −4.4 [49%], and −1.7 [17%], respectively; ( P = .04 )). Mean baseline DQOLS Symptoms scales were 43.4, 44.5, and 50.9 for the 0.075-mg/kg alefacept, 0.025-mg/kg alefacept, and placebo groups. Mean change in DQOLS Symptoms scale [% improvement] were significantly greater in patients receiving 0.025- and 0.075-mg/kg alefacept compared with placebo (21.1 [47%], 19.4 [45%], and 8.2 [16%], respectively; ( P = .01 )).</td>
</tr>
<tr>
<td>Gordon et al 85 (2003)</td>
<td>Efalizumab</td>
<td>556 pts with stable, moderate to severe plaque psoriasis</td>
<td>DLQI</td>
<td>Mean baseline DLQI was 11.9 for alefacept 15-mg group compared with 10.9 for the placebo group. Mean reductions from baseline in DLQI scores were significantly greater in the alefacept 15-mg group than in the placebo group 2 wk after last dose (−4.9 vs −2.7 points; ( P = .012 )). Similar observations were made for DQOLS and SF-36 scores in favor of alefacept 2 wk and 12 wk after last dose.</td>
</tr>
<tr>
<td>Gottlieb et al 37 (2003)</td>
<td>Etanercept</td>
<td>112 pts with moderate to severe plaque psoriasis</td>
<td>DLQI</td>
<td>Mean percent improvement in DLQI score was 64% in 25-mg twice-weekly SC etanercept group compared with 7% for placebo control (( P &lt; .001 )) at week 12.</td>
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<tr>
<td>Chan and Gebauer 88 (2003)</td>
<td>Infliximab</td>
<td>7 pts with chronic plaque psoriasis</td>
<td>DLQI</td>
<td>A single dose of infliximab (5 mg/kg IV) induced 61% improvement in DLQI scores at wk 2.</td>
</tr>
<tr>
<td>Menter et al 10† (2002)</td>
<td>Alefacept</td>
<td>&gt;1000 pts with psoriasis from two phase III clinical trials</td>
<td>DLQI, DQOLS</td>
<td>Four of 7 pts were seen at 10 wk after infusion and sustained improvement in DLQI (79%) ( P &lt; .001 ). Pts receiving 7.5 mg IV or 15 mg IM alefacept reported mean improvements in DLQI of 4.4 and 4.9 points vs mean placebo improvements of 1.8 points (( P &lt; .0001 )) and 2.7 points (( P &lt; .001 )), respectively.</td>
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</tr>
</thead>
<tbody>
<tr>
<td>Touw et al\textsuperscript{87} (2001)</td>
<td>CsA</td>
<td>255 pts with chronic plaque psoriasis</td>
<td>DLQI</td>
<td>Patients receiving 7.5 mg IV alefacept reported significant mean improvements in DQOLS scores vs placebo as assessed by the Psychosocial (10.8 vs 6.1; ( P = .005 )), Activities (10.4 vs 4.9; ( P &lt; .0001 )), and Symptoms (19.9 vs 9.2; ( P &lt; .0001 )) scales</td>
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<tr>
<td>Gupta et al\textsuperscript{94} (1999)</td>
<td>Narrowband UVB</td>
<td>100 consecutive pts with chronic plaque, small plaque, or guttate psoriasis</td>
<td>PDI</td>
<td>Median DLQI scores improved from 36.67% of maximum score at baseline to 3.33% at end of the 12-wk therapy, for a mean change of (-9.58 ) (( P &lt; .001 ))</td>
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\textsuperscript{89}Menter A, Hamilton T, Caro I, Chen-Rundle A. Impact of efalizumab on patient-reported outcomes in patients with moderate to severe plaque psoriasis: pooled results from three randomized phase III trials. Results from two randomized, placebo-controlled phase III trials.


\textsuperscript{92}Wallace K, Hamlin R, Langley R, Chen DM. Results of the Dermatology Life Quality Index in moderate to severe plaque psoriasis patients receiving 12 weeks of adalimumab therapy. Presented at the 10th International Psoriasis Symposium, June 10-13, 2004; Toronto, Canada.


\textsuperscript{94}Mease and Menter.
a questionnaire on two sides of one page that comprises a patient-reported assessment on one side and a physician-reported evaluation on the other. Patients are asked to assess psoriasis-specific HRQOL (PQOL-12), location and extent of the disease, and the presence of and degree of arthritis symptoms, based on their experience in the previous month. The PQOL-12 is a 12-item scale derived from a 41-item psoriasis quality of life questionnaire and was chosen as the quality of life measure for the KMPI because of its brevity, broad applicability, the rigor of its development and psychometric validation, and its psoriasis-specific focus. Each item in the PQOL-12 is rated on a 0 to 10 scale for a maximum score of 120, with higher scores indicative of worse quality of life and a score of 50 representing significant negative HRQOL because of psoriasis.

In a study of 474 psoriatic patients, the KMPI was determined to be a valid and reliable instrument for assessing the impact of psoriasis across a wide ranging spectrum of disease severity. It is responsive and sensitive to changes in disease after treatment, as recently demonstrated in a trial of tazarotene therapy (Table III). Each item in the PQOL-12 is rated on a 0 to 10 scale for a maximum score of 120, with higher scores indicative of worse quality of life and a score of 50 representing significant negative HRQOL because of psoriasis.

To demonstrate its validity, the PDI was compared to 5 other measures, namely the PASI, the SF-36, and the DLQI. The PDI was shown to have moderate correlation with the PASI, the SIP, and the SF-36; and high correlation with the DLQI and the GHQ. PDI scores declined after ultraviolet phototherapy, which shows its sensitivity and responsiveness to the treatment (Table III). However, a major limitation of the PDI is its suboptimal sensitivity to changes in patients with mild to moderate disease.

The Psoriasis Life Stress Inventory. The Psoriasis Life Stress Inventory (PLSI) is a 15-item instrument designed to measure psoriasis-related stress associated with cosmetic disfigurement and social stigma, symptoms of disease, and treatment effects (Table II). It is derived from a 41-item questionnaire based on a study of 50 psoriatic patients. Each item is rated on a 0 to 3 scale for a maximum score of 45, based on their experience in the previous month. Higher scores indicate poorer quality of life.

Compared with the PDI, the PLSI provides a better measurement of HRQOL in patients with mild to moderate psoriasis because of its greater emphasis on psychosocial stressors. It has been validated against the SF-36 and the PDI. Demonstrated that patients with higher stress levels had lower mental health (measured by the SF-36) and experienced more disability (measured by the PDI) than patients with less stress. However, the sensitivity of the PLSI to changes in HRQOL after treatment has not been assessed. The instrument only has modest correlation with global patient self-ratings, but no correlation with the PASI.

The Salford Psoriasis Index. The Salford Psoriasis Index (SPI) is one of the more recently developed tools in psoriasis that assesses 3 aspects of the disease: signs of psoriasis based on the current PASI score, psychosocial disability, and historical severity of psoriasis as judged by the need for intervention (Table II). The SPI score is converted into a number from 0 to 10, reflecting the extent of the disease. Psychosocial disability is measured using a visual analogue scale from 0 to 10, and historical severity is graded by assigning points (0 to 5) to patients who had previous systemic treatment, who were hospitalized, and who experienced erythroderma as a result of their disease. The SPI is then expressed as 3 independent values. For example, a 1:1:0 score would indicate minimal signs, psychosocial impact, and historical severity, whereas a 10:10:0 score represents serious impairment in HRQOL.

In a study assessing 150 consecutive patients with psoriasis, the individual components of the SPI were validated against each other and against the PASI and the PDI. A modest correlation was found among all 3 components. The Psychosocial Impact Score


correlated strongly with the PDI, but not with the PASI. To demonstrate reliability and sensitivity, the SPI was assessed in two separate cohorts. The SPI showed high reproducibility and was highly responsive to changes in HRQOL after treatment for psoriasis. These findings were corroborated in a subsequent trial of 101 patients with psoriasis.97

**Other quality-of-life instruments currently in development.** As described earlier, the PsAQOL measure, a 20-item questionnaire, has recently been developed by McKenna et al66 specifically for measuring HRQOL in patients with PsA. It was designed to provide a convenient and practical tool that allows arthritic and dermatological impacts to be summarized in a single outcome measure. A 25-item measure specific to psoriasis (PSORIQoL) has also been developed using the same needs-based quality-of-life model adopted for the PsAQOL.69 The premise for the needs-based quality-of-life model is that disease-related disability can influence the patient’s ability to meet his or her needs. Both instruments have been shown to have good internal consistency, test-retest reliability, and validity.66,69 However, they have not yet been tested in clinical trials to assess their responsiveness to changes in HRQOL associated with treatments.

**IMPROVING QUALITY OF LIFE: TREATMENT OF PSORIASIS AND PSORIATIC ARTHRITIS**

It is important to understand that HRQOL instruments provide not only assessments of the impact of a disease but also its treatment. Studies demonstrating significant improvements in HRQOL have been very limited for older therapies, such as phototherapy and traditional systemic therapy. This is primarily because until now these treatments have only been modestly used as monotherapy, especially in patients with moderate to severe disease, and many have not been satisfactory with respect to either safety or efficacy.6,23a,4 In addition, many of these agents were available well before the treatment paradigm placed a greater emphasis on quality of life. The advent of the biologics has substantially improved treatment options and coincided with this shift toward a more global approach in evaluating treatment efficacy. Improvements in HRQOL have recently been demonstrated with various agents, ranging from traditional phototherapy and systemic treatments to biologic therapies (Table III). In all of these studies, patients experienced a concomitant improvement in PASI scores.

Significant improvements in HRQOL have also been observed with nonbiologic therapies (Table III). A 12-week course of oral tazarotene, a novel receptor-selective retinoid, resulted in a significant improvement in PQOL-12 scores compared with placebo (1.63 vs −0.84).‡ Narrowband ultraviolet phototherapy was also effective in improving HRQOL, with significant reductions in PDI scores observed after 3 months of treatment (from a baseline score of 42 to 30 at 3 months).94 Treatment with leflunomide, a pyrimidine-inhibiting agent, was associated with significantly greater improvement in DLQI scores (−1.9 units) compared with placebo (−0.2 units).98 In addition, the leflunomide-treated patients demonstrated significant improvement in HAQ scores, with a mean change of 0.19 unit observed at week 24, compared with only 0.05 unit for the placebo control.98 Intermittent short courses of cyclosporine monotherapy produced an even greater decline in DLQI scores after 12 weeks (mean change, −9.58)97 and was shown to have efficacy comparable to that of methotrexate in improving SF-36 scores among patients with moderate to severe psoriasis.39 Despite significant improvements in both disease severity and quality of life, the majority of older therapies are characterized by cumulative toxicity (methotrexate, cyclosporine), brief duration of posttreatment remission (topical medications, methotrexate and cyclosporine treatment), and inconvenient administration modalities (ultraviolet phototherapy) that limit their potential for long-term maintenance therapy.

Alefacept, efalizumab, and etanercept are 3 biologic drugs that have recently been approved in the United States for the treatment of psoriasis and are in different stages of development for approval in the rest of the world. Alefacept (Amevive) is a recombinant dimeric fusion protein consisting of the

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Salonen SH on behalf of the EUROPSo Patient Survey Study Group. The EUROPSo psoriasis patient study: Treatment history and satisfaction reported by 17,990 members of European psoriasis patient associations. The EUROPSo Psoriasis Patient Study. Presented at the 1st European Academy of Dermatology and Venereology Spring Symposium, Feb 27-March 1, 2003, Malta.

CD2-binding portion of the human leukocyte function antigen-3 protein linked to the Fc region of human immunoglobulin G1 (IgG1).\textsuperscript{99} In 3 independent trials of patients with chronic plaque psoriasis, alefacept provided a modest, but consistent improvement in HRQOL, as measured by the DLQI and the DQOLS (Table III).\textsuperscript{70,71,75} Mean changes in DLQI scores were significantly greater in the alefacept group (ranging from $-3.4$ to $-4.9$) at 12 weeks after the last dose, compared with placebo (ranging from $-1.4$ to $-2.7$). In these studies, reductions in DQOLS scores were similarly higher in the alefacept treatment group compared with the placebo group, indicating improvement in quality of life. Patients receiving either weekly intravenous or intramuscular administration of alefacept reported similar improvements, with positive effects observed as early as 2 weeks.\textsuperscript{73} However, alefacept therapy currently requires 12 weekly physician visits for routine monitoring of lymphocyte counts (CD4) and intramuscular injections of the drug, thus requiring time off from work.\textsuperscript{99}

Efalizumab (Raptiva) is a recombinant humanized IgG1 $\kappa$ isotype monoclonal antibody that binds specifically to human CD11a.\textsuperscript{100} After 12 weeks of treatment with subcutaneous efalizumab at a dosage of 1 mg/kg per week, mean reduction in DLQI score was $-5.6$ units, compared with $-1.9$ units for the placebo control.\textsuperscript{86,87} When expressed as a percentage, mean improvement in DLQI was 46% versus 15% for the placebo group. Almost identical rates were observed in another study, in which mean DLQI improvement of 47% was reported for efalizumab-treated patients, compared with only 14% for placebo-treated patients.\textsuperscript{85} Efalizumab therapy requires infrequent monitoring of platelet counts because of rare instances of drug-induced thrombocytopenia.\textsuperscript{85,100}

TNF antagonists are another class of biologics that have been successfully used in treating rheumatic diseases, and have subsequently been shown to be effective in treating both psoriasis and PsA.\textsuperscript{16,37,74,75,85,88,89} With better safety profiles than traditional agents. Currently, there are 3 TNF-neutralizing agents, a soluble TNF-receptor antagonist (etanercept)\textsuperscript{101} and two monoclonal antibodies (infliximab and adalimumab).\textsuperscript{102,103} Of these 3, etanercept has thus far been approved for use in the treatment of both psoriasis and PsA.

Etanercept (Enbrel) is a fully human soluble TNF-receptor IgG1 fusion protein that inactivates the biological activity of endogenous TNF by competitively inhibiting its interaction with cell-surface receptors.\textsuperscript{101} Mean percent improvement in DLQI scores was highly significant and dose-dependent after etanercept therapy in patients with moderate to severe psoriasis (Table III). In one study, subcutaneous etanercept, 25 mg given twice weekly, induced an impressive 64% mean improvement in DLQI score compared with only 7% for the placebo group.\textsuperscript{87} Gradual improvement in DLQI was observed over a 60-week period in another study, from 39% at week 24 to 51% at week 36, and 54% at week 60.\textsuperscript{84} Krueger et al\textsuperscript{86} showed that statistically significant improvements in DLQI scores were apparent as early as 2 weeks and increased with time and dosage of etanercept. At week 12, mean improvement in DLQI was 70% for 50 mg twice-weekly etanercept.


\textsuperscript{1}Menter A, Hamilton T, Caro I, Chen-Rundle A. Impact of efalizumab on patient-reported outcomes in patients with moderate to severe plaque psoriasis: pooled results from three randomized phase III trials. Results from two randomized, placebo-controlled phase III trials. Presented at the 62nd Annual Meeting of the American Academy of Dermatology, Feb 6-11, 2004, Washington, DC.


\textsuperscript{1}Feldman SR, Kimball A, Woolley JM, Zitnik R. Clinically meaningful improvements in health-related quality of life from etanercept therapy for patients with moderate to severe psoriasis. Presented at the 62nd Annual Meeting of the American Academy of Dermatology, Feb 6-11, 2004, Washington, DC.


65% for 25 mg twice-weekly etanercept, and 6% for placebo. Reductions in DLQI scores corresponded to similar improvements in SF-36 scales. Comparable improvements were reported in a pivotal trial of etanercept, in which mean improvement in DLQI was 74% for the 50-mg twice-weekly etanercept group, 59% for the 25 mg twice-weekly etanercept group, and 54% for the 25 mg once-weekly etanercept group, compared with only 11% in the placebo group.16

Infliximab and adalimumab are monoclonal anti-TNF antibodies that are currently in phase III clinical trials for the treatment of psoriasis (Table III). Infliximab (Remicade) is a chimeric monoclonal antibody to TNF that combines the variable region of a mouse antibody with the constant region of a human IgG1 antibody.102 In a case study report of 7 patients with chronic plaque psoriasis, a single dose (5 mg/kg) of intravenous infliximab induced a 61% improvement in DLQI scores at 2 weeks.88 Improvement was sustained for up to 10 weeks (79% improvement in DLQI). In a trial of 249 patients with extensive to severe plaque psoriasis, a median improvement of 91% (−10.0 units from baseline) and 84% (−8.0 units from baseline) was observed at week 10 for the 5- and 3-mg/kg infliximab groups, respectively, compared with 0% (0.0 units from baseline) for the placebo group.4 Adalimumab (Humira) is a recombinant human IgG1 monoclonal antibody to TNF.103 In a large phase II trial of adalimumab, patients with psoriasis were recently reported to show significantly greater mean change in DLQI after receiving either 40 mg adalimumab every other week (−10.8 units) or 40 mg adalimumab weekly (−11.5 units), compared with placebo (−1.3 units).†

Among patients with refractory PsA, a significant improvement in the HAQ was demonstrated in patients treated with etanercept at week 24.74,75,†‡ A mean change of 0.6 unit in the HAQ (54%) was found in patients receiving twice-weekly 25-mg etanercept, compared with only 0.1 unit (6%) for the placebo group.74,75,†‡ In addition, 50% of patients in the etanercept group compared with 14% in the placebo group achieved a 0.5 unit improvement, which represents a clinically meaningful change. These improvements were corroborated by other measures, including the SF-36 and the EUROQOL Feeling Thermometer (Table III). In a 12-month observational study, infliximab therapy led to a marked improvement in psoriasis (as measured by the PASI), but did not show statistically significant improvement in either the HAQ or the SF-36.72 However, this study was based on a small sample size of only 16 PsA patients. HRQOL results from larger completed clinical trials of infliximab and adalimumab therapies in patients with PsA are expected to be published soon.

CONCLUSIONS

A review of the literature on psoriasis and PsA demonstrates the significant adverse effects that the diseases have on quality of life. New therapies are emerging that have greatly improved patients’ quality of life, as well as the ability to control skin and joint disease, which therefore behooves us to more accurately measure this domain as well as other more clinical disease domains. On the basis of our survey of the literature, it is quite apparent that there is currently a lack of uniformity in how HRQOL is measured in patients with psoriasis and PsA. Individual differences in the various instruments, and even in the way improvements are represented (either as a unit or a percentage), prevent true cross-study comparisons that allow patients and physicians to determine which therapies provide the greatest benefit. Although treatment efficacy is usually measured by changes in the PASI and other physician-reported instruments, they do not always provide a complete picture of the patient’s health status. As treatments have become increasingly more effective in treating skin conditions, optimal therapy that leads to long-lasting remission can only be achieved by addressing both the physical and psychosocial ill effects of these disorders. Several drug therapies reduce the severity of skin lesions, but may not necessarily improve the patient’s psychosocial well-being. In fact, treatments that have significant adverse effects (eg, requiring regular physician and laboratory visits) and high costs can improve a patient’s physical appearance, but may lead to occupational and financial distress. Traditional medications such as methotrexate may also cause gastrointestinal side effects and a feeling of malaise for 24 to 48 hours after each weekly dose. Biologic therapies represent more effective treatments for many psoriasis patients because they can dramatically improve multiple facets of a patient’s


life, including the physical, psychological, social, and occupational domains of HRQOL. The TNF inhibitors particularly are of benefit because of their effectiveness in both skin and joint aspects of psoriasis.

Measures of quality of life often claim to be able to capture all psychosocial dimensions associated with specific illnesses. However, there is currently no “gold standard” measure in dermatology. This will require refinement of existing instruments and a consensus-building process similar to OMERACT, with the goal being the standardization of assessment tools. The initial work of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis and the International Psoriasis Council is encouraging in this regard, and standardization is likely to be accomplished in the years ahead with the close cooperation of dermatologists and rheumatologists.

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REFERENCES


