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The psychosocial burden of psoriatic arthritis

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ABSTRACT

Objective: To assess the psychosocial impact of psoriatic arthritis (PsA), describe how health-related quality of life (QoL) is affected in patients with PsA, discuss measures used to evaluate the psychosocial impact of PsA, and review studies examining the effect of therapy on QoL.
Methods: A targeted review on the impact of PsA on QoL and the role of tailored psychosocial management in reducing the psychosocial burden of the disease was performed. PubMed literature searches were conducted using the terms PsA, psychosocial burden, QoL, and mood/behavioral changes. Articles were deemed relevant if they presented information regarding the psychosocial impact of PsA, methods used to evaluate these impacts, or ways to manage/improve management of PsA and its resulting comorbidities. The findings of this literature search are descriptively reviewed and the authors' expert opinion on their interpretation is provided.
Results: The psychosocial burden of PsA negatively affects QoL. Patients suffer from sleep disorders, fatigue, low-level stress, depression and mood/behavioral changes, poor body image, and reduced work productivity. Additionally, each patient responds to pain differently, depending on a variety of psychological factors including personality structure, cognition, and attention to pain. Strategies for evaluating the burdens associated with PsA and the results of properly managing patients with PsA are described.
Conclusions: PsA is associated with a considerable psychosocial burden and new assessment tools, specific to PsA, have been developed to help quantify this burden in patients. Future management algorithms of PsA should incorporate appropriate assessment and management of psychological and physical concerns of patients. Furthermore, patients with PsA should be managed by a multidisciplinary team that works in coordination with the patient and their family or caregivers.

Introduction

Psoriatic arthritis (PsA) is a systemic inflammatory arthritis that is associated with skin psoriasis. In patients with PsA, not only are the skin and joints affected but periarticular structures tend to be more affected, including tendons and ligaments, causing classic exam findings of dactylitis and enthesitis [1]. PsA affects between 0.04% and 1% of the general population and patients are typically aged 30–55 years at disease presentation [2,3]. Furthermore, PsA is equally prevalent in men and women [3]. PsA and psoriasis share similar pathogenic mechanisms and it is common for individuals to develop both conditions [4]. In the majority of patients with PsA (up to 85%), psoriasis develops many years before joint symptoms occur, while approximately 15–25% of patients present with concomitant skin and joint symptoms [5]. Additionally, up to 90% of patients with PsA have nail involvement that results in pitting, ridging, and distal onycholysis [1,3]. In most patients, skin and nail changes precede joint or spinal symptoms [5]. The exact cause of PsA is unknown; however, multiple components appear to contribute to its pathogenesis, including genetic, immunologic, and environmental factors [1]. Although there are many similarities to rheumatoid arthritis (RA), PsA is now known to be a distinct form of inflammatory arthritis.

Patients with PsA have significantly poorer health-related quality of life (QoL) than the general population [6–10]. In contrast to RA, where the skin is not involved, involvement of 2 chronic conditions (i.e., psoriasis and arthritis) that affect both the skin and joints can result in both functional and cosmetic concerns for many patients with PsA. Similarly, compared with psoriasis alone, PsA is associated with worse QoL and patients with PsA have

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worse functional status and greater disability than those with psoriasis alone [8,11–13]. The presence of concurrent psoriasis can confound the impact of PsA because psoriasis is also associated with a high burden of illness [14]. Further, the impact of psoriasis is more than cosmetic; with suicidal ideation being reported in approximately 10% of patients aged 18–34 years [15].

This review examines how QoL is impacted in patients with PsA, and discusses how appropriate management of patients can lessen the psychosocial burden. The contributions of chronic disease manifestations, personality traits, patient perceptions, fatigue, and depression are highlighted. Evaluation of PsA-related distress, as well as unmet needs in the treatment of the psychosocial burden associated with PsA will also be discussed.

Methods

PubMed literature searches were conducted to review the impact of QoL on PsA and studies focusing on disease management in reducing the psychosocial burden of patients with PsA. Searches were conducted using combinations of search terms including PsA, psychosocial burden, QoL, and mood/behavioral changes. Search results were supplemented based on the reference citations in articles identified in initial searches and based on the authors' knowledge of the field. Articles were deemed relevant if they presented information regarding the psychosocial impact of PsA, methods used to evaluate these impacts, or ways to manage/improve management of PsA and its resulting comorbidities. The findings of this literature search are descriptively reviewed and the authors' expert opinion on their interpretation is provided.

Psychosocial burden of PsA

Quality of life

In addition to the effects of the disease itself, patients with PsA have more comorbidities than the general population, with over 50% of patients having at least 1 comorbidity [10,16,17]. Important comorbidities in patients with PsA include cardiovascular disease, ophthalmic disease, liver disease, inflammatory bowel disease, depression and anxiety, osteoporosis, kidney disease, malignancy, and infection [17]. Cardiovascular disease is the leading cause of death in patients with PsA, and is responsible for 20–56% of deaths [16]. These extensive comorbidities certainly also impact QoL. In fact, when compared to other cohorts, such as individuals with psoriasis alone, individuals with PsA have significantly poorer QoL [18].

Body image

The cosmetic effects of psoriasis on social burden and the functional effects of arthritis are well documented [7,19]. The QoL impairment observed in patients with psoriasis is comparable to that found in individuals with other chronic disease including heart disease, diabetes, cancer, and depression [20]. Additionally, the visibility of psoriasis can result in poor psychosocial function in patients with PsA, causing embarrassment, self-consciousness, and depression [7,21]. Patients feel stigmatized by the disease, reporting feelings of rejection, shame, and guilt [19]. Psoriasis is also associated with sexual dysfunction, especially for patients with genital/inverse involvment that is more commonly found in individuals with PsA [22,23].

Psychological factors influencing pain

Pain is defined as both a sensory and emotional experience [24], supporting attention to psychological factors and a multidimensional conceptualization of the individual with PsA. Personality structure, cognitions, emotions, lifestyle factors, and psychiatric comorbidities must all be considered when approaching treatment of individuals with PsA.

Personality

The personality of a patient can affect the coping responses they employ in responding to the stress of having a chronic condition [25]. Coping with chronic inflammatory arthritis has been described as a dynamic, iterative, balancing process that requires patients to redefine what is considered as normal life throughout the course of their disease [26]. Specifically, increased symptoms of pain, fatigue, and stiffness result in patients paying more attention to how they are being affected by the disease and making efforts to ease disease symptoms [26]. People who tend to be perfectionists or have rigid personalities may not cope well with chronic conditions. In particular, research has demonstrated that self-critical tendencies and perfectionism may play an important role in the onset and perpetuation of chronic pain disorders [27,28].

Individuals with certain personality styles may also respond less robustly to educational and multidisciplinary treatment programs for pain [27]. Furthermore, personality disorders may complicate the treatment of chronic pain conditions, impacting coping style and also increasing the risk of other psychiatric comorbidities. A recent systematic review supports the finding that personality disorders are common among individuals with chronic pain conditions, with borderline, and obsessive–compulsive, personality traits being the most common [29]. Moreover, individuals with comorbid personality disorders and chronic pain show higher rates of overall healthcare utilization [29].

Cognition and attention to pain

One's interpretation of a stressor such as pain significantly modifies the pain experience. For example, appraisal of pain as “excruciating” or an experience of unbearable or never-ending suffering amplifies the pain experience. Similarly, the amount of attention and importance placed upon pain is a significant factor in the averseness of the experience. These findings are supported by animal studies showing that brain cells in areas such as the rostroventral medulla that function to amplify incoming pain signals at the level of the dorsal horn, are activated simply by the anticipation of pain and holding an expectation that it is important [30].

Psychological theories, such as cognitive-behavioral theories of pain, depression, and stress, support the direct association between belief/interpretations, emotions, coping responses, and overall pain. One specific style of thinking, pain catastrophizing, defined as a negative cognitive–affective response to anticipated or actual pain, has been repeatedly linked to overall worse outcome in acute and chronic pain [31]. The impact of pain in PsA is emphasized by the bidirectional association between pain and depression in patients with PsA [32]. Additionally, when occurring together, pain and depression are reported to be more important predictors of disability and QoL than radiographic joint damage and disease activity in rheumatic diseases [33,34].

Sleep and fatigue

Patients with PsA also commonly suffer from sleep disorders, fatigue, and low-level stress, which have a considerable impact on QoL [35–39]. Combined pain, fatigue, and anxiety can create a vicious cycle, which can worsen symptoms and the impact of PsA [38]. It has also been suggested that irritability and low energy levels caused by a lack of sleep may cause patients to withdraw from favored activities, and fatigue may lead to reduced activity

and poor physical fitness [38]. Furthermore, multiple studies confirm a reciprocal relationship with sleep and pain, with compelling support that a night, or repeated nights, of poor sleep worsen pain ratings overall for the patient [40].

Depression and mood/behavioral changes

Anxiety and concern about bodily symptoms have been shown to be independent correlates of physical health-related QoL [41]. In both acute and chronic pain conditions, negative emotions, particularly anger and anxiety, have been repeatedly associated with increases in pain. Uncontrolled anxiety often leads to a response of avoidance. In an individual with pain, such as experienced in PsA, this can contribute to physical and emotional suffering through inactivity/deconditioning and social isolation. Also, patients with PsA have a high risk for depression, which appears to be greater than for patients with psoriasis [42]. In a cross-sectional study that included 83 patients with PsA, Kotsis et al. [41] observed moderate-to-severe depressive symptoms in 22% of participants. Although depression is more common in patients with PsA than in those without PsA, the presence of PsA does not result in a higher rate of suicidal behavior [43]. Assessment for the presence of comorbid depression is important because adherence to treatment may be more difficult in these patients [38].

While increased risk of depression in patients with PsA may be due to the psychosocial difficulties associated with having a disfiguring skin condition that causes reduced QoL, the risk of depression may also be linked to the pathogenesis of PsA. New evidence suggests an inflammatory etiology of depression, rather than a simple imbalance of monoamine neurotransmitters. Pro-inflammatory cytokines involved in the pathogenesis of PsA such as interleukin (IL)-6, IL-17, and tumor necrosis factor (TNF)-α have also been associated with symptoms of depression and anxiety [44–46]. The relationship between the pathophysiology of depression and PsA offers the possibility of treatment parallels by targeting similar pro-inflammatory cytokines. For example, an observational study found a significant decrease in prevalence of depression and insomnia in patients with psoriasis (80% with concomitant PsA) following biologic therapy targeting TNF-α [47]. Future studies are needed to clarify the relationship between the pathophysiology and treatment of PsA and depression so that patients can be properly evaluated and managed.

Occupation/work productivity

The combination of pain, fatigue, and anxiety experienced by patients with PsA can contribute to work absenteeism and increased disability can result in lost productivity and unemployment [7,38,39,48,49]. Additionally, the decreased physical functioning associated with PsA can impact the self-worth of patients. In a systematic literature review, patients with PsA were found to have high levels of unemployment (20–50%) and work disability (16–39%), which were impacted by longer disease duration, worse physical function, a high number of affected joints, low educational level, female gender, erosive disease, and manual work [50]. Other studies demonstrated that work productivity as evaluated by the Work Limitations Questionnaire (WLQ) was decreased by 4.3–6.7% in patients with PsA compared with benchmark employees without limitations [48,51]. Disease duration of 2–5 years has been observed to negatively influence remaining in employment [odds ratio (OR) = 0.41; 95% confidence interval (CI): 0.180–0.953; $P = 0.03$], with the risk of unemployment increasing with worsening physical function [i.e., for every 1-point increase in Health Assessment Questionnaire (HAQ) score, the risk of unemployment is increased by an OR of 0.56 (95% CI: 0.343–0.926; $P = 0.02$)] [49]. In this study, employer helpfulness also affected whether patients remain employed. Individuals with PsA that rated an employer as helpful had an increased likelihood of employment (OR = 15.10; 95% CI: 4.658–69.355; $P \leq 0.01$), even if the individual did not think that they needed help (OR = 3.22; 95% CI: 1.264–8.229; $P < 0.01$) [49].

PsA is also associated with significant economic burdens to patients and society. It is estimated that yearly indirect costs of work disability account for $10,754 per individual in 2013 prices in the United States and direct and indirect costs resulting from PsA have been shown to increase with worsening physical function and disease activity [7,52].

Evaluating psychosocial burden in patients with PsA

Evaluation of patients with PsA should include assessment of psychological parameters such as depression and anxiety, in addition to overall functioning. Social and family support available to the patient should be evaluated via the clinical interview. This discussion should include inquiry into familial relationships, the impact of pain on these relationships and the family's responses to the individual's pain. Studies suggest that PsA has a negative impact on the QoL of family members, and that divergent beliefs about the disease or solicitous responses from family and/or significant others may increase patient distress, pain intensity, physical disability, and pain behaviors [53–56]. The last decade has seen a rapid development of outcome measures in PsA and outcome measures have been validated for disease activity in individual key domains including arthritis, skin, enthesitis, and dactylitis [57,58]. With regards to assessment tools for the evaluation of psychosocial burden in patients with PsA, validated questionnaires exist such as the Short Form-36 (SF-36) mental component summary and the Psoriatic Arthritis Quality of Life (PsAQoL) instrument, but some assessments may be difficult for most physicians to implement in routine clinical practice due to their complexity [57]. Also, it is important to interview the patient because patients may minimize responses on paper questionnaires. Patient mannerisms should be observed to detect possible functional concerns that may not be captured verbally [59]. Collateral information from family and friends can also be valuable, particularly when “red flags” such as minimized depression, anxiety, pyschosocial stress, or substance use are present.

Physical functioning

HAQ is a commonly used measure of physical functioning across many different forms of arthritis, which has been demonstrated to be simple, accurate, and practical [60]. Also, the Pain Disability Index (PDI), which measures the degree to which pain disrupts aspects of life across 7 different life domains (family/home responsibilities, recreation, social activity, occupation, sexual behavior, self-care, and life-support activity), has been proven to be a brief, valid, and reliable measure of pain-related disability [61].

Dermatology-specific metrics

Dermatology-specific metrics such as the Dermatology Life Quality Index (DLQI) [62] should also be considered for patients with PsA who have skin involvement. Some measures of psoriasis do not include itch as a metric. Thus, it is important to evaluate itch since it is considered the most bothersome symptom in patients with psoriasis, and it can affect a patient's physical and psychosocial outcome [63,64]. The Psoriasis Area and Severity Index (PASI) measures the impact of psoriasis by body region and includes scores for erythema, induration, and scaling, as well as

evaluation of body surface area affected for each region, and is a validated instrument for the effect of treatment on psoriasis [65].

Sleep and fatigue

For the assessment of fatigue and sleep disorders, the Functional Assessment of Chronic Illness Therapy-fatigue (FACIT-fatigue) scale has been validated in PsA [66]. Also, an algorithm for the evaluation and treatment of sleep disorders associated with rheumatologic diseases including seronegative spondyloarthropathies has been developed [67].

Depression and anxiety

Several scales are useful for the measurement of depression and anxiety in patients with PsA. The Depression, Anxiety and Stress Scale (DASS-21) has 3 subscales (depression, anxiety, and stress), and is reliable, free to use, and easy to administer [68]. It also measures irritability and tension, which are important factors in the evaluation of pain. The Patient Health Questionnaire-9 (PHQ-9) is a valid instrument for the assessment of depression based on the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria [41]. It has been used to assess the prevalence of moderate-to-severe depressive symptoms and psychological distress in patients with PsA but, because symptoms of depression may change over time and PHQ-9 only assesses symptoms during the preceding 2 weeks, its reliability is uncertain. The Goldberg Anxiety and Depression scale-7 (GAD7) is a brief, efficient, and validated tool for the measurement of anxiety that has been suggested for use in patients with PsA to identify those who should be referred to a specialist for possible emotional disorders [69,70].

Quality of life

Generic measures of QoL [SF-36, EuroQol 5 domain (EQ-5D)] have been validated in PsA [57,71]. DLQI is used for the assessment of QoL in patients with both PsA and psoriasis. In the recently updated Core Domain set, outcome measures in rheumatology (OMERACT) recommends that health-related QoL should be measured in all PsA trials [35].

The PsA Impact of Disease (PsAID) is a recently developed tool for assessing patient-reported outcome measures in patients with PsA [37]. It was developed by the European League Against Rheumatism (EULAR) with the aim of fully capturing the impact of PsA from the patient's perspective. PsAID comprises domains considered by patients to be most impacted by the disease (i.e., pain, fatigue, skin problems, work and/or leisure activities, functional capacity, discomfort, sleep disturbance, coping, anxiety, embarrassment and/or shame, social participation, and depression). While initial impressions are that the questionnaire will prove valuable both in clinical practice and clinical trials, further validation is needed.

Additional measures

New research has been conducted into composite measures of psoriatic disease, including response measures and proposed cut-off points for disease activity [58]. Assessment scales include the Composite Psoriatic Disease Activity Index (CPDAI), the PsA Disease Activity Score (PASDAS), the Disease Activity in Psoriatic Arthritis (DAPSA) score, and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) Composite Exercise (GRACE) index. CPDAI was considered the first true composite measure of disease activity, and, with this measure, both disease activity and impact are assessed for each disease domain (peripheral arthritis, skin disease, enthesitis, dactylitis, and axial disease).

Clinical studies evaluating patient-reported social outcomes

There has been an increase in the measurement of fatigue and QoL concerns in clinical trials, which has demonstrated that therapies have beneficial effects on physical and mental functioning, and QoL (Table). Caution should be used in making comparisons between these studies due to the use of differing methodologies between clinical trials.

Approved agents, such as the TNF inhibitor certolizumab pegol, the IL-12/23 inhibitor, ustekinumab, and the phosphodiesterase 4 inhibitor, apremilast, are effective for the treatment of PsA, as well as improving QoL in patients failing disease-modifying antirheumatic drugs (DMARDs) and other TNF inhibitors [86]. Similarly, phase 3 trials of the recently approved IL-17A inhibitor secukinumab have shown efficacy in treating PsA and improving QoL in both TNF inhibitor-naïve patients and those with an inadequate response to prior TNF-targeting therapy [82,83]. Ixekizumab, another IL-17A inhibitor, has shown efficacy for PsA and improvement in QoL in biologic-naïve patients and a trial in patients with inadequate response to prior TNF-targeting therapy is in progress (NCT02349295) [84].

While most of these newer, targeted, agents showed improvements in HAQ-Disability Index (DI) and SF-36 scores (mental and physical components), few agents (certolizumab pegol) have been assessed using PsA-specific measures of QoL (Table). Certolizumab pegol is widely studied with regard to the effects of treatment on psychosocial burden of PsA, showing significant improvements vs placebo in both general measures of QoL (HAQ-DI, SF-36 physical and mental component scores) as well as PsA-specific measures of QoL (PsAQoL, DLQI), and improved productivity (fewer working days missed and fewer days with $\geq$50% reduced work productivity due to arthritis) (Table) [78,79].

Unmet needs in treating the psychosocial burden of PsA

Delay in diagnosis and treatment

Prompt diagnosis and treatment of PsA is important for preventing progressive and irreversible joint damage and disability [1,87–89]. However, there are no definitive laboratory tests (e.g., screening antibody tests) or x-ray tests for the early diagnosis of PsA and the Classification Criteria for Psoriatic Arthritis (CASPAR) classification criteria require the presence of inflammatory arthritis (joint, spine, or enthesis) for accurate diagnosis [1,38,90].

PsA is generally more difficult to diagnose than RA [1]. A lack of awareness for PsA symptoms among patients, primary care physicians, and dermatologists, can delay referral of a patient to a rheumatologist [38]. Subsequently, delayed diagnosis can lead to a delay in receiving the most efficacious treatment and patients with PsA often experience a 2 – 3 year delay in diagnosis compared with those with RA [91]. This delay in diagnosis results in further functional decline and bone erosion [1,87,89,92]. Delays in the treatment of PsA may also negatively impact mental health due to increased functional limitations and decreased QoL [89].

Nontreatment and undertreatment of PsA is a significant problem in the United States [93]. Many clinicians have the misconception that PsA has a milder course than RA and does not require aggressive treatment; however, recent studies confirm PsA as a progressive and disabling arthropathy with consequences as severe as RA [94]. Further complicating diagnosis and initiation of treatment, is the lack of a well-developed treatment algorithm for PsA. Treatment

Table
Studies of newer targeted therapies in patients with PsA reporting QoL data

Phase (study name)	Agent and dose	*N*	QoL results
TNF-alpha inhibitors			
Mease et al. [72]	• Etanercept 25 mg BIW • Placebo	60	HAQ-DI of 0 at wk 12 • Placebo: 3% • Etanercept: 34%
Phase IV (PRESTA) Kirkham et al. [73]	• Etanercept 50 mg QW	103	• Mean change from baseline to wk 24 in patients with PsA ≤ 2 vs > 2 years • Joint pain: −42.1 vs −34.6 ($P = 0.007$) • Arthritis activity: −41.7 vs −34.9 ($P = 0.01$) • EQ-5D utility: +0.30 vs +0.24 ($P = 0.046$) • EQ-5D VAS: +22.8 vs +18.7 ($P = 0.04$) • HAQ: −0.52 vs −0.49 (ns) • HADS anxiety: −2.1 vs −2.0 (ns) • HADS depression: −1.6 vs −1.6 (ns) • Morning stiffness: −103.8 vs −95.0 (ns) • Sick days: −0.9 vs −1.0 (ns) • Employed: 59.8% vs 59.7% (ns)
Phase IV (PRISTINE) Thaçi et al. [74]	• Etanercept 50 mg QW (QW/QW) • Etanercept 50 mg BIW → 50 mg QW (BIW/QW)	270	Sleep scores at wk 12 • Etanercept QW/QW: 30.8 • Etanercept BIW/QW: 30.1 Sleep scores at wk 24 • Etanercept QW/QW: 28.4 • Etanercept BIW/QW: 28.2 Sleep improvement was associated with improved EQ-5D utility and FACIT-F ($P < 0.001$)
Phase III (IMPACT 2) Antoni et al. [75]	• Infliximab 5 mg/kg • Placebo	200	Change in SF-36 PCS at wk 24: • Placebo: 1.3 • Infliximab: 7.7 ($P = 0.001$) Change in SF-36 MCS at wk 24 • Placebo: 0.4 • Infliximab: 3.9 ($P = 0.047$)
Phase III (ADEPT) Mease et al. [76]	• Adalimumab 40 mg q2w • Placebo	315	Change in HAQ DI at wk 24 • Placebo: −0.1 • Infliximab: −0.4 ($P < 0.001$) Change in SF-36 PCS at wk 24 • Placebo: 1.4 • Infliximab: 9.3 ($P < 0.001$) Change in SF-36 MCS at wk 24 • Placebo: 0.6 • Infliximab: 1.8 (ns)
Phase III (GO-REVEAL) Kavanaugh et al. [77]	• Golimumab 50 mg or 100 mg q4w • Placebo	405	Change in HAQ DI at wk 24 • Placebo: −0.01 • Golimumab: −0.36 ($P < 0.001$) Change in SF-36 PCS at wk 24 • Placebo: 0.67 • Golimumab: 7.83 ($P < 0.001$) Change in SF-36 MCS at wk 24 • Placebo: −0.6 • Golimumab: 3.84 ($P < 0.001$) Impact of disease on productivity at wk 24 • Placebo: 0.08 • Golimumab: 2.24 ($P < 0.001$)
Phase III (RAPID-PsA) Gladman et al. [78]	• Certolizumab pegol 200 mg q2w • Certolizumab pegol 400 mg q2w • Placebo	409	Change in HAQ DI at wk 24 • Placebo: −0.17 • Certolizumab pegol 200 mg: −0.52 ($P < 0.001$) • Certolizumab pegol 400 mg: −0.43 ($P < 0.001$) Change in SF-36 PCS at wk 24 • Placebo: 2.1 • Certolizumab pegol 200 mg: 8.4 ($P < 0.001$) • Certolizumab pegol 400 mg: 7.6 ($P < 0.001$)

Table (*continued*)

Phase (study name)	Agent and dose	*N*	QoL results
Gladman et al. [78]			Change in SF-36 MCS at wk 24 • Placebo: 0.7 • Certolizumab pegol 200 mg: 5.5 ($P < 0.001$) • Certolizumab pegol 400 mg: 3.5 ($P < 0.05$) Change in PsAQoL at wk 24 • Placebo: −1.3 • Certolizumab pegol 200 mg: −4.4 ($P < 0.001$) • Certolizumab pegol 400 mg: −3.3 ($P < 0.0010$) Change in DLQI at wk 24 • Placebo: −1.4 • Certolizumab pegol 200 mg: −6.3 ($P < 0.001$) • Certolizumab pegol 400 mg: −5.2 ($P < 0.0010$)
Phase III (RAPID-PsA) Kavanaugh et al. [79]	• Certolizumab pegol 200 mg q2w • Certolizumab pegol 400 mg q2w • Placebo	409	Mean work days missed due to arthritis • Placebo: 2.6 • Certolizumab pegol 200 mg: 2.0 • Certolizumab pegol 400 mg: 1.6 Mean days with ≥50% reduced work productivity due to arthritis • Placebo: 3.8 • Certolizumab pegol 200 mg: 5.2 • Certolizumab pegol 400 mg: 5.1 Mean rate of arthritis interference with work productivity • Placebo: 4.2 • Certolizumab pegol 200 mg: 4.4 • Certolizumab pegol 400 mg: 3.8
Interleukin-12/23 inhibitor Phase III (PSUMMIT 1) McInnes et al. [80]	• Ustekinumab 45 mg • Ustekinumab 90 mg • Placebo	615	Change in HAQ-DI at wk 24 • Placebo: 0 • Ustekinumab 45 mg: −0.25 ($P < 0.0001$) • Ustekinumab 90 mg: −0.25 ($P < 0.0001$) Change in SF-36 MCS at wk 24 • Placebo: 0.3 • Ustekinumab 45 mg: 2.7 ($P = 0.0654$) • Ustekinumab 90 mg: 4.4 ($P = 0.0010$) Change in SF-36 PCS at wk 24 • Placebo: 1.2 • Ustekinumab 45 mg: 3.9 ($P < 0.0001$) • Ustekinumab 90 mg: 5.8 ($P < 0.0001$) Change in DLQI at wk 24 • Placebo: −1.0 • Ustekinumab 45 mg: −6.0 ($P < 0.0001$) • Ustekinumab 90 mg: −6.0 ($P < 0.0001$)
Phase III (PSUMMIT 2) Ritchlin et al. [81]	• Ustekinumab 45 mg • Ustekinumab 90 mg • Placebo	312	Change in HAQ-DI at wk 24 • Placebo: 0 • Ustekinumab 45 mg: −0.13 ($P < 0.01$) • Ustekinumab 90 mg: −0.25 ($P < 0.001$) Change in SF-36 MCS at wk 24 • Placebo: 0 • Ustekinumab 45 mg: 0.7 • Ustekinumab 90 mg: 2.2 Change in SF-36 PCS at wk 24 • Placebo: 0 • Ustekinumab 45 mg: 2.7 ($P < 0.01$) • Ustekinumab 90 mg: 3.5 ($P < 0.01$) Change in FACIT-F at wk 24 • Placebo: 0 • Ustekinumab 45 mg: 3.0 ($P < 0.01$) • Ustekinumab 90 mg: 3.0 ($P < 0.01$)

Table (*continued*)

Phase (study name)	Agent and dose	*N*	QoL results
Ritchlin et al. [81]			Change in DLQI at wk 24 • Placebo: 0 • Ustekinumab 45 mg: −6.0 ($P < 0.001$) • Ustekinumab 90 mg: −6.0 ($P < 0.001$)
Interleukin-17 inhibitor			
Phase III (FUTURE 1) Mease et al. [82]	• Secukinumab 75 mg • Secukinumab 150 mg • Placebo	606	Change in HAQ-DI at wk 24 • Placebo: −0.17 • Secukinumab 75 mg: −0.41 ($P < 0.001$) • Secukinumab 150 mg: −0.40 ($P < 0.001$) Change in SF-36 PCS at wk 24 • Placebo: 1.82 • Secukinumab 75 mg: 5.41 ($P < 0.001$) • Secukinumab 150 mg: 5.91 ($P < 0.001$)
Phase III (FUTURE 2) McInnes et al. [83]	• Secukinumab 75 mg • Secukinumab 150 mg • Secukinumab 300 mg • Placebo	397	Change in HAQ-DI at wk 24 • Placebo: −0.31 • Secukinumab 75 mg : −0.32 • Secukinumab 150 mg: −0.48 ($P = 0.0555$) • Secukinumab 300 mg: −0.56 ($P = 0.0040$) Change in SF-36 PCS at wk 24 • Placebo: 1.95 • Secukinumab 75 mg: 4.38 • Secukinumab 150 mg: 6.39 ($P = 0.0057$) • Secukinumab 300 mg: 7.25 ($P = 0.0013$)
Phase III (SPIRIT-P1) Mease et al. [84]	• Ixekizumab 80 mg q2w • Ixekizumab 80 mg q4w • Adalimumab 40 mg q2w • Placebo	417	Change in HAQ-DI at wk 24 • Placebo: −0.18 • Ixekizumab 80 mg q2w: −0.50 ($P \leq 0.001$ vs placebo) • Ixekizumab 80 mg q4w: −0.44 ($P \leq 0.001$ vs placebo) • Adalimumab 40 mg q2w: −0.37 ($P \leq 0.01$ vs placebo) Change in SF-36 PCS at wk 24 • Placebo: 2.9 • Ixekizumab 80 mg q2w: 8.2 ($P \leq 0.001$ vs placebo) • Ixekizumab 80 mg q4w: 7.5 ($P \leq 0.001$ vs placebo) • Adalimumab 40 mg q2w: 6.8 ($P \leq 0.01$ vs placebo)
Oral phosphodiesterase 4 inhibitor			
Phase III (PALACE 1) Kavanaugh et al. [85]	• Apremilast 20 mg BID • Apremilast 30 mg QD • Placebo	504	Change in HAQ-DI at wk 24 • Placebo: −0.08 • Apremilast 20 mg: −0.21 ($P = 0.0092$) • Apremilast 40 mg: −0.26 ($P = 0.0004$) Change in SF-36 PCS • Placebo: 1.5 • Apremilast 20 mg: 3.5 ($P = 0.0295$) • Apremilast 30 mg: 5.1 ($P = 0.0001$)

Abbreviations: BID, twice daily; BIW, twice weekly; DLQI, Dermatology Life Quality Index; EQ-5D, EuroQOL-5D; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HADS, Hospital Anxiety and Depression Scale; HAQ-DI, Health Assessment Questionnaire Disability Index; MCS, Mental Component Score; ns, not statistically significant; PCS, Physical Component Score; PsA, psoriatic arthritis; PsAQoL, Psoriatic Arthritis Quality of Life Questionnaire; q2w, every 2 weeks; q4w, every 4 weeks; QD, daily; QoL, quality of life; QW, once weekly; SF-36, Short Form-36; TNF, tumor necrosis factor; VAS, visual analog scale; wk, week.

recommendations for PsA have largely been borrowed from other inflammatory arthritis treatment protocols such as RA trials, and current treatment guidelines are based on studies with lower levels of evidence [95]. Evidence related to psychological factors and treatments in patients with PsA is also limited and largely borrowed from research in treating other chronic pain conditions. The goals of treatment for PsA should include early diagnosis, with early aggressive treatment aimed at halting or minimizing joint damage and clearing the skin of psoriasis [88,95]. Recently published GRAPPA treatment guidelines reiterate that optimal management of patients with PsA remains a major challenge, and highlight the need for better identification and prompt treatment of patients as a key area for future research [95]. Additonally, these guidelines emphasize key clinical domains (arthritis, spondylitis, enthesitis, dactylitis, skin, and nail disease) of interest in PsA and advise that treatment should be geared toward these domains.

Lack of data for nonbiologic DMARDs

Compared with the relative wealth of data on the effects of biologics on psychosocial outcomes, data for traditional nonbiologic DMARDs are lacking. Approved in the United States for the treatment of severe psoriasis, methotrexate is a widely used first-line treatment for PsA despite a lack of data confirming its efficacy [96,97]. In illustration, a 6-month, randomized, double-blind study of methotrexate vs placebo in 212 patients with active PsA showed

no evidence of a significant treatment effect on joint counts, erythrocyte sedimentation rate, C-reactive protein level, pain scores, or HAQ scores after 3 or 6 months of treatment [96]. In the methotrexate arm of the TICOPA trial, improvement occurred in pain, fatigue, global disease activity, PsAQoL, and HAQ, but, due to study design, these findings could not be compared with placebo or an active comparator [98]. Additionally, comparative data regarding the effects of biologic versus nonbiologic DMARDs on psychosocial outcomes are needed.

Lack of patient education

While various treatment modalities are available for PsA, there is still widespread treatment dissatisfaction among patients [93]. Patients with rheumatic diseases are not satisfied with the level of information that they receive about their treatments, diagnosis, or how to improve daily activities [39]. Thus, efforts should be made to help patients gain a better understanding of their condition and how to manage it.

Discussion: The future landscape of PsA treatment practices

Practical tips/clinical insight in caring for patients with PsA and psychosocial issues

It is our belief that PsA and its associated pain cannot be effectively treated without addressing all of the psychosocial factors mentioned above. Thus, treatment must integrate all of these factors and be comprised of an interdisciplinary team to improve patient outcomes (Fig.).

Patients must be educated about the rationale for this treatment approach and be in agreement with the physician before initiating treatment. Psychological and physical concerns ideally should be managed simultaneously, and in coordination with other healthcare providers [70]. Initial screening can be performed by a physician, and identified patients should then be referred to a psychologist trained in pain. As PsA is a chronic condition, the process of evaluation and re-evaluation of patients should be a continuous one [88]. Function and disability should also be routinely assessed. Patients should be offered, and educated about, the range of available treatments, and advised of new treatment options. Also, patients should be empowered to cope on their own, with support from a psychologist during more difficult times.

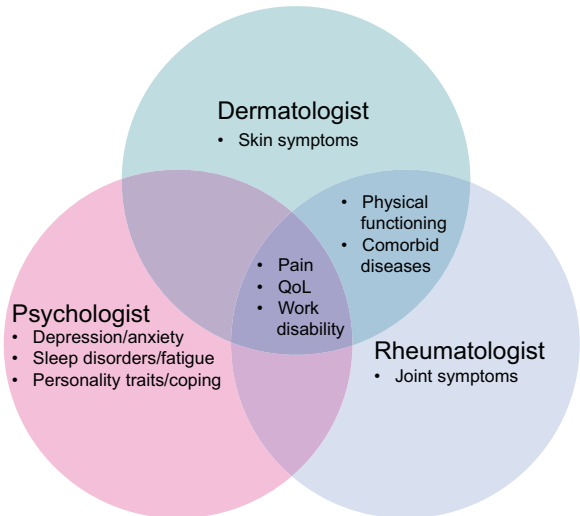

Fig. Integrated approach to treatment of patients with psoriatic arthritis (PsA) and its psychosocial burden.

Clinical trials

There is also the need for clinical trials to include evaluation of QoL concerns. Racial differences in disease severity, psychosocial impact, and response to treatment have been observed in patients with PsA [99]. To guide policy, studies are required to evaluate the impact of early diagnosis and treatment on outcome, according to disease phenotype [94]. A core set of clinical variables, which should be taken into account when considering patients affected by PsA, and assessment tools most suitable for measuring disease activity and/or severity in clinical practice, have recently been recommended by a joint dermatologist–rheumatologist board [70]. Recommended measures included PASI, Nail Psoriasis Severity Index, and DLQI for assessment of psoriasis; 68/66 tender/swollen joints count, PASDAS, Bath Ankylosing Spondylitis Disease Activity Index, CPDAI, and Leeds Enthesitis Index for assessment of psoriatic arthritis; count number for dactylitis; and assessment of comorbidities (cardiovascular disease, metabolic syndrome, uveitis, and anxiety/depression). Additionally, an update to the PsA core domain set was recently endorsed by OMERACT following a systematic literature review of outcomes used in PsA studies and group consensus agreement of patients and physicians [100,101]. Agreement was reached that evaluation of pain, patient's global assessment, physical function, health-related QoL, and fatigue should be included in all studies and it was highly recommended that emotional well-being, participation, and economic cost should be included in studies [100,102]. It was also decided that investigation of instruments to measure these factors should be undertaken to develop a core outcome measurement set [100].

Conclusions

PsA is associated with a considerable psychosocial burden and new assessment tools, specific to PsA, have been developed to better quantify this burden in patients. Studies of newer biologic therapies in patients with PsA have shown significant improvement in patient-reported outcomes and QoL measures. Furthermore, future management algorithms of PsA should incorporate appropriate assessment and management of psychological and physical concerns of patients. Ideally, patients with PsA should be managed by a multidisciplinary team including rheumatologists, primary care physicians, and, when appropriate, dermatologists, psychiatrists, mental health therapists, and behavioral health providers. The team of providers should work in coordination with both the patient and their family or caregivers.

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