Treatment guidelines for psoriatic arthritis

Psoriatic arthritis is a chronic, disabling disease. Therapies for psoriatic arthritis have been borrowed from rheumatoid arthritis and spondyloarthritis. Traditional DMARDs have shown little effect and there is no evidence that any of these drugs prevented disease progression. Although anti-TNF agents have shown efficacy on symptoms and radiographic progression, these new agents are expensive and not available to all patients. In an attempt to standardize and rationalize their use many national rheumatology associations have set guidelines for the use of these therapies. Recently, the Group of Research and Assessment of Psoriasis and Psoriatic Arthritis, an international group of rheumatologists, dermatologists, and methodologists developed a new set of guidelines. The main advantage of this guideline is that it takes into account all aspects of psoriatic disease, including skin, nail and axial involvement, enthesis and dactylitis. Here we analyze these different guidelines and highlight their strengths and limitations.

KEYWORDS: anti-TNF agents ■ clinical guideline ■ psoriasis ■ psoriatic arthritis

Enrique R Soriano
Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires & Fundacion Pedro M. Catoggio, Gascon 450, Capital Federal (1181), Argentina
Tel.: +54 114 959 0378;
Fax: +54 114 959 0378;
enrique.soriano@hospitalitaliano.org.ar

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Learning objectives

Upon completion of this activity, participants should be able to:

- Describe the epidemiology and prognosis of psoriatic arthritis
- Identify the class of medications most likely to slow the progression of psoriatic arthritis
- List treatment strategies for psoriatic arthritis
- Describe elements of the recommended evaluation of patients with psoriatic arthritis

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Author & Credentials

Enrique Roberto Soriano, MSC, MD, *Rheumatology Section, Internal Medicine Service, Hospital Italiano de Buenos Aires, and Fundacion Pedro M. Catoggio, Argentina*

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CME Author

Charles P Vega, MD, FAAFP, Associate Professor; Residency Director, Department of Family Medicine, University of California, Irvine, CA, USA

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Psoriatic arthritis (PsA) is a chronic inflammatory disease that affects between 0.02 and 0.4% of the population with an equal sex distribution [1]. Psoriasis affects 1–3% of the population, with approximately a third of patients developing PsA [2].

Initially PsA was felt to represent rheumatoid arthritis (RA) occurring coincidentally with psoriasis. The work of Wright [3–5] and Baker [6], helped to distinguish both diseases, but it was not until 1964 that, for example, the American College of Rheumatology (GA, USA) (previously the American Rheumatism Association) adopted PsA as a distinct clinical entity, including it in a classification of rheumatic diseases [7].

Psoriatic arthritis is classified among the spondyloarthropathies because of the presence of spinal and sacroiliac involvement in about 50% of patients and presence of extra-articular features common to spondyloarthropathies such as enthesitis, as well as the association with *HLA-B*27* and negative rheumatoid factor.

Although the course of PsA is variable and unpredictable, erosive and deforming arthritis occurs in 40–60% of PsA patients, and is progressive from within the first year of diagnosis [2,8–10]. Predictors for disease progression include polyarticular presentation, as well as the degree of joint inflammation [10,11]. PsA leads to chronic joint damage, increased disability [12,13] and increased mortality [14]. For all these reasons joint inflammation in PsA must be treated appropriately to control patients' symptoms as well as to prevent progression of damage.

Therapies for PsA have been borrowed from RA and spondyloarthritis [15,16]. Nonsteroidal anti-inflammatory medications may control symptoms, but they have no effect on joint damage progression. Traditional DMARDs have shown little effect and there is no evidence that any of these drugs actually prevented disease progression [15,16]. In Table 1 the effect of these drugs is summarized. For sulfazalasine, ciclosporin and leflunomide there is evidence grade 1A for improvement of symptoms, but there is no evidence of prevention of radiographic progression. For methotrexate (MTX), the evidence is even weaker for disease control (grade 2B) and again no evidence of halting radiographic progression. As shown in Table 1 the effect size of all these drugs is very small (effect size is the standardized mean difference between a treatment group and a control group for a given outcome variable. Effect sizes of 0.2 or less are considered small, whereas effect sizes greater than 0.8 are considered large [15]) (Table 1).

More recently the introduction of anti-TNF agents including etanercept, infliximab and adalimumab for the treatment of PsA has shown remarkable results [15,17–19]. In addition to controling signs and symptoms of joint inflammation, the anti-TNF agents have shown a potential to prevent progression of radiological damage [18,20–22]. Anti-TNF have also shown remarkable efficacy on skin involvement in patients with severe refractory skin disease (Table 1) [23–26].

The new, effective agents for PsA are very expensive and they are not readily available to all patients, especially in developing countries. In order to standardize and rationalize the use of this medications many national healthcare authorities as well as insurance companies have approached national rheumatology associations to help set guidelines for the use of these expensive therapies [16]. In many countries with national health systems the guidelines are mandatory.

All these guidelines are mainly for the use of anti-TNF in PsA. These guidelines are reviewed in the following sections.

Table 1. Summary on efficacy and toxicity for standard DMARDs and anti-TNF agents in psoriatic arthritis.

Measures of efficacy/toxicity	SSZ	MTX	CyA	LFN	ETN	INF	ADL
Grade of evidence on JSC	1A	2B	1B	1B	1B	1B	1B
Effect size* on JSC	Small	Small	Med	Small	–	Large	–
Grade of evidence on x-ray progression	-3	-3	3	4	1B	1B	1B
Grade of evidence on SSC involvement	1B	1B	1B	1B	1B	1B	1B
Effect size on SSC	–	Med	Large	Med	Large	Large	Large
Toxicity	Low	Low	High	Low	Low	Low	Low
Recommendation grade for PsA	A	B	A	A	A	A	A

Grade of evidence and recommendation according to Agency for Health Care Policy Research [48].
**Effect size is the standardized mean difference between a treatment group and a control group for a given outcome variable* [15]. *Effect sizes of 0.2 or less are considered small, whereas effect sizes greater than 0.8 are considered large.*
ADL: Adalimumab; CyA: Ciclosporin; ETN: Etanercept; INF: Infliximab; JSC: Joints symptom control; LFN: Leflunomide; Med: Medium; MTX: Methotrexate; PsA: Psoriatic arthritis; SSC: Skin symptom control; SSZ: Sulfazalasine.

National guidelines for the use of anti-TNF agents in PsA

Canadian Rheumatology Association guideline

The first guidelines were published in 2003, by the Canadian Rheumatology Association (Ontario, Canada). This set was aimed to the use of anti-TNF agents in spondyloarthritis, but included a section on PsA [27]. Following a systematic literature review they recommended that anti-TNF use be based on the decision of the physician and patient, taking into consideration the degree of inflammation and stage of disease. Recently these guidelines were updated [28]. The updated guideline suggested that sulfasalazine and MTX may be considered in patients with peripheral arthritis, particularly psoriatic spondyloarthritis, in doses up to 3 g per day and 25 mg weekly, respectively (TABLE 2). The guidelines stated that anti-TNF therapy should be offered to those with persisting inflammation (either synovitis or enthesitis) despite a trial of NSAID therapy and one DMARD (either MTX or sulfasalazine) [28]. One of the limitations of this guideline is that it did not provide a definition of persisting inflammation, nor did it provide suggested tools for the assessment of disease activity or response to therapy for peripheral involvement. As this guideline was targeting spondyloarthritis, treatment and assessment tools for axial involvement were much better specified. Nonpharmacological treatment including patient education, regular exercise, individual and group physical therapy and taking NSAIDs were recommended as first-line treatment for patients with axial involvement with pain and stiffness. The Canadian guideline stated that anti-TNF treatment should be offered to those with persisting symptoms despite a trial of NSAID therapy (at least three NSAIDs, each administered over a minimum 2-week period at accepted maximum dosage if tolerated) and evidence of active disease as defined by at least two of the following: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of 4 or more [29], elevated C-reactive protein and/or erythrocyte sedimentation rate, inflammatory lesions in the sacroiliac joints and/or spine appearing in MRI [27,28]. There was no mention of other clinical manifestations of PsA.

British Society of Rheumatology guideline

The British Society of Rheumatology (London, UK) also developed guidelines for use of anti-TNF therapy in PsA patients (TABLE 2) [30]. The authors acknowledged the lack of evidence to strongly support the use of standard DMARDs (MTX, sulfasalazine, ciclosporin A and leflunomide) but despite this, anti-TNF-α was recommended only after failure of adequate therapeutic trials of at least two of the above DMARDs, individually or in combination. They further recommend that continued use be based on evidence for improvement within 3 months [30]. In this case active disease was defined as three or more tender and three or more swollen joints on two separate occasions at least 1 month apart, based on a 78 tender and 76 swollen joint count. Dactylitis was recommended to be counted as one active joint, but enthesitis was not covered by the guideline [30]. This group recommended the use of the PsA Responder Criteria [31] as the primary joint response tool. The PsA Responder Criteria is a response criterion adapted from the Veteran Affairs Cooperative Study of sulfazalazine that includes: tender joint count, swollen joint count, patient global health and physician global health [31]. PsA axial only disease was not included in British guidelines, referring those interested to British Society of Rheumatology guideline for prescribing TNF-α blockers in adults with ankylosing spondylitis.

French Society for Rheumatology guideline

The French Society for Rheumatology (Paris, France) published recommendations on the use of TNF-α antagonist therapy in ankylosing spondylitis and PsA (TABLE 2) [32,33]. This group of experts recommended Moll and Wright criteria for the diagnosis of PsA and defined standard DMARD therapy of at least 4 months of MTX in a dosage of 15 mg/week or more, leflunomide 20 mg/day or more, or sulfasalazine 2 g/day or more. TNF-α antagonist therapy could be considered when at least one of these three DMARDs proves inadequately effective, defined as persistent active disease. Active disease was defined as presence of at least three tender and swollen joints (66 out of 68 joints in all). As response criteria for anti-TNF treatment this working group elected more than 30% decrease in the tender/swollen joint count [32,33]. For predominantly axial disease, active disease was defined as a BASDAI of 4 out of 10 or more. In axial disease TNF-α antagonist therapy were recommended after failure of conventional treatment defined as an inadequate response to at least three NSAIDs taken in optimal tolerated dosages for at least 3 months [33]. Inadequate response to anti-TNF agents was defined as less than two points' improvement on the 10 point BASDAI scale.

Table 2. Comparison of different guidelines for the treatment of psoriatic arthritis.

Guideline	Publication year	Targeted audience	Targeted disease	NSAID therapy	Standard DMARD therapy	Time to failure (months)	Number of DMARDs before anti-TNF	Anti-TNF without previous DMARD	Time for anti-TNF failure	Ref.
Canadian Rheumatology Association	2003–2007	Insurance payers, formularies, government agencies, healthcare providers in addition to rheumatologists	Spondyloarthritis	At least three NSAIDs, 2 weeks, each at maximum dose	Sulfasalazine methotrexate	3	1	Yes, in predominant axial disease	16 weeks	[27,28]
British Society of Rheumatology	2005	Rheumatologists and prescribing clinicians	PsA, peripheral involvement	Not stated	Sulfasalazine methotrexate ciclosporin leflunomide	6	2	No (axial disease not included)	3 months	[30]
French Society for Rheumatology	2006	Rheumatologists	ankylosing spondylitis and PsA	At least three NSAIDs, optimal tolerated dosages for at least 3 months	Methotrexate leflunomide sulfasalazine	4	1	Yes, in predominant axial disease	6–12 weeks	[32]
Italian Society for Rheumatology	2006	Rheumatologists	PsA	Two NSAIDs over 3 months	Methotrexate ciclosporin sulfasalazine leflunomide	3	2	Yes, in predominant axial disease	3 months	[34]
American Academy of Dermatology	2008	Not clearly stated	PsA	Not stated	Methotrexate sulfasalazine leflunomide	Not stated	0–1	Yes, in severe disease	Not stated	[36]
GRAPPA	2008	All clinicians who care for PsA patients	PsA	Not stated	Sulfasalazine leflunomide methotrexate ciclosporin	3	1	Yes, in predominant axial or severe disease	Not stated	[37]

GRAPPA: Group for Research and Assessment of Psoriasis and Psoriatic Arthritis; PsA: Psoriatic arthritis.

Italian Society for Rheumatology guideline

In 2006 the Italian Society for Rheumatology (Milan, Italy) published their own recommendations for the use of biologic (TNF-α blocking) agents in the treatment of PsA (**Table 2**) [34]. Salvarani *et al.* divided assessment and recommendations into three subsets depending on the predominant involvement: PsA with peripheral arthritis, PsA characterized by enthesitis and psoriatic spondylitis. For PsA with peripheral arthritis they proposed that anti-TNF-α agents be considered for active PsA in patients who are resistant to NSAIDs and at least two conventional disease-modifying antirheumatic drugs. In cases of oligo/monoarthritis and/or enthesitis, it was suggested that anti-TNF-α agents should only be considered for patients who are also resistant to at least two local steroid injections [34]. They considered standard DMARD therapy: MTX, ciclosporin, sulfasalazine or leflunomide, administered alone or in combination for at least 3 months (defined: full therapeutic doses 2–3 g per day for sulfasalazine, 20 mg per week for MTX, 3–5 mg per kg/body weight per day for ciclosporin, and 20 mg per day for leflunomide). The Italians defined peripheral active disease as at least one swollen and three tender joints [34]. These guidelines were the first ones to provide specific therapeutic recommendations for enthesitis. This working party recommended that anti-TNF therapy should be considered in patients with PsA characterized predominantly by peripheral enthesitis if they have not responded over a 3-month period to maximal doses of at least two NSAIDs and at least two DMARDs as well as to local steroid therapy (at least two steroid injections), and an expert agrees, plus they have at lease two points of tenderness over inflamed entheses on a 0–4 Likert scale and BASDAI 40 mm (visual analog scale: 0–100 mm) [34].

For patients with psoriatic spondylitis (sacroiliitis and/or spondylitis) this group recommended that anti-TNF-α therapy should be considered if they have not responded over a 3-month period to maximal doses of at least two NSAIDs, plus favorable expert opinion and BASDAI of greater than 4 [34].

Response assessment was also very well defined in this guideline. Recommendation was given to use the following tools to assess response to anti-TNF agents: tender joint count; swollen joint count; pain on visual analog scale; patient's global assessment of disease activity; physical function (Health Assessment Questionnaire); Maastricht Ankylosing Spondylitis Enthesis Score (MASES [for patients with enthesitis]); BASDAI (for patients with spinal involvement); indices of spinal mobility (Schober's test, spinal lateral flexion, chest expansion, cervical spine flexion and tragus-to-wall distance) (for patients with spinal involvement); and an expert opinion [34].

American Academy of Dermatology guideline

Recently a group of experts in psoriasis from the USA within the American Academy of Dermatology (IL, USA) published a set of guidelines of care for the management of psoriasis and PsA [35,36]. This is an extensive and comprehensive review on the diagnosis, classification, assessment and treatment of psoriasis and PsA (**Table 2**). This group recommended that upon diagnosis of PsA, patients should be treated and/or referred to a rheumatologist to alleviate signs and symptoms, inhibit structural damage, and improve quality of life (QOL) parameters [36]. According to the authors' MTX, TNF blockade, or the combination of these therapies is considered first-line treatment for patients with moderate to severely active PsA. The authors stated that not all patients with PsA require treatment with MTX or TNF blockade. Patients with mild PsA can be successfully treated with NSAIDs or intra-articular injections of corticosteroids [36]. Although axial involvement, enthesitis and dactylitis were included in the efficacy review, specific recommendations on their treatment were not included [36]. A number of assessment tools available were carefully reviewed in this paper, although not one was specifically recommended [36].

Regarding skin involvement the guideline included a decision tree [35]. For patients without PsA and limited skin disease the decision tree suggested topicals and/or targeted phototherapy [35]. For patients with extensive disease without PsA psoralen plus ultraviolet (PUVA), systemic treatments or biologics were included. For those patients with PsA the decision tree suggested TNF inhibitors although patients with nondeforming PsA without any radiographic changes, loss of range of motion, or interference with tasks of daily living should not automatically be treated with TNF inhibitors, according to American Academy of Dermatology experts [35].

The limitation of most of these guidelines is that they are only referred to the use of anti-TNF-α agents mainly in peripheral PsA involvement. For that reason the Group of Research and

Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) decided to develop guidelines for the treatment of PsA taking into account all other disease manifestations (including skin, peripheral joints, axial involvement, nails, and enthesis and dactylitis)[37].

International treatment recommendations for psoriatic arthritis: GRAPPA guideline

The Group of Research and Assessment of Psoriasis and Psoriatic Arthritis is an international group of rheumatologists, dermatologists and methodologists committed to research, treatment and improvement of patients with psoriatic disease [38]. To address the need for evidence-based treatment recommendations, members of GRAPPA published systematic reviews of the literature to identify the best available evidence regarding treatment of the various manifestations of PsA [15,25,26,39–42]. Treatment recommendations were formulated by rheumatologists and dermatologists in GRAPPA in conjunction with PsA patients, based on evidence from these systematic reviews and consensus opinion. These recommendations were developed to provide the best care for patients with PsA, regardless of economic or political considerations [37].

Severity assessment in PsA

In an attempt to assist the treating physician in decision making, patients were roughly stratified in categories of mild, moderate or severe for peripheral arthritis, skin disease, spinal disease, enthesitis and dactylitis according to presence of criteria noted in Table 3. Usually patients have multiple manifestations, and treatment decisions may be determined by the most severe clinical presentation [37].

Peripheral arthritis

For all patients with moderate or severe peripheral arthritis as defined in Table 3 initiation of therapy with standard DMARDs was recommended (sulfasalazine, leflunomide, MTX or ciclosporin). For patients who fail to respond to at least one DMARD any of the 3 currently available TNF inhibitors (etanercept, infliximab or adalimumab) were recommended. Accoring to GRAPPA guidelines, patients with poor prognosis could be considered for TNF inhibitors even if they have not failed a standard DMARD therapy (Table 2) [37].

Spinal disease

For patients with mild-to-moderate disease (Table 3), NSAIDs, physiotherapy, education, analgesia and injection of sacroiliac joint were suggested. For patients who fail therapies for mild-to-moderate disease, taking into account that infliximab, etanercept and adalimumab have demonstrated efficacy in ankylosing spondylitis, the consensus was that similar treatment responses were also likely to be observed in axial PsA [37], and that these therapies could be recommended.

Enthesitis

For mild or moderate enthesitis, NSAIDs, physical therapy and/or corticosteroids were recommended. For those patients failing therapy or with severe enthesitis GRAPPA suggests the use of TNF inhibitors [37].

Table 3. Disease Severity according to GRAPPA guideline.

Disease manifestation	Mild	Moderate	Severe
Peripheral arthritis	<5 joints No damage on x-ray No LOF QOL-minimal impact Pt evaluation mild	≥5 joints (S or T) Damage on x-ray IR to mild Rx Moderate LOF Moderate impact on QOL Pt evaluation moderate	≥5 joints (S or T) Severe damage on x-ray IR to mild–moderate Rx Severe LOF Severe impact on QOL Pt evaluation severe
Skin disease	BSA < 5, PASI < 5, asymptomatic	Nonresponse to topicals, DLQI, PASI < 10	BSA > 10, DLQI > 10, PASI > 10
Spinal disease	Mild pain No loss of function	Loss-of-function or BASDAI > 4	Failure of response
Enthesitis	1–2 sites No loss-of-function	>2 sites or loss-of-function	Loss of function or >2 sites and failure of response
Dactylitis	Pain absent to mild Normal function	Erosive disease or functional loss	Failure of response

BASDAI: Bath ankylosing spondylitis disability activity index; BSA: Body surface area; DLQI: Dermatology life quality index; GRAPPA: Group of Research and Assessment of Psoriasis and Psoriatic Arthritis; IR: Inadequate response; LOF: Loss of function; PASI: Psoriasis activity severity score; QOL: Quality of life; Pt: Patient; Rx: Treatment (e.g., NSAIDs, DMARDs, physiotherapy, steroid injection, analgesia and so on); S: Swollen; T: Tender.
Reproduced with permission from [37].

Dactylitis

For dactylitis the lack of evidence is striking. The consensus was to suggest NSAIDs and injected steroids. For resistant disease DMARDs were recommended although changing to anti-TNF agents (infliximab) where some evidence is available should be considered according to GRAPPA guideline [37].

In Figure 1, GRAPPA treatment guidelines for PsA, categorized by disease characteristics and distinct organ involvement are summarized.

Skin

Unusual clinical subsets of psoriasis can co-occur with arthritis; thus, treatment may vary from that used in psoriasis vulgaris [37]. For erythrodermic/generalized pustular psoriasis, GRAPPA guideline suggested acitretin as first-line therapy [37]. For palmoplantar pustuolosis acitretin and oral PUVA with combination of the two as providing superior response were considered. For treatment of hand/foot psoriasis the suggestion was to consider topical PUVA, soriatane or efalizumab as preferable first-line agents [37].

A warning that aggressive immunosuppression should not follow extensive phototherapy (especially PUVA), given the increased risk of melanoma and nonmelanoma skin cancer in this scenario, was given [37].

All three TNF inhibitors were recommended for severe disease [37]. The fact that in some psoriasis studies, etanercept efficacy was dose-dependent, with doses as high as 100 mg per week (double the typical dose for RA and PsA patients) providing the most benefit, was specially mentioned [37].

The lack of evidence of efficacy for all treatments for nail disease was also pointed out [37]

Diagnosis & assessment

Classification criteria for PsA (CASPAR) criteria were recommended for diagnosis of PsA (Box 1) [43].

For baseline PsA assessment the use of the core set of domains established at Outcome Measures in Rheumatology (OMERACT) 8 was strongly supported (Figure 2) [44]. The assessment includes the following domains:

- Peripheral joint assessment (68 joints for tenderness; 66 joints for swelling);
- Pain (patient reported on a visual analog or category rating scale);
- Patient global assessment of disease activity;
- Physical function (e.g., as measured by the Health Assessment Questionnaire);
- Health-related QOL, as assessed by a general measure (e.g., short form 36 [SF-36]) or a PsA-specific measure (e.g., Psoriatic Arthritis QOL [PsAQOL]);
- Fatigue, measured by patient self-report or a general instrument (e.g., Functional Assessment of Chronic Illness Therapy);

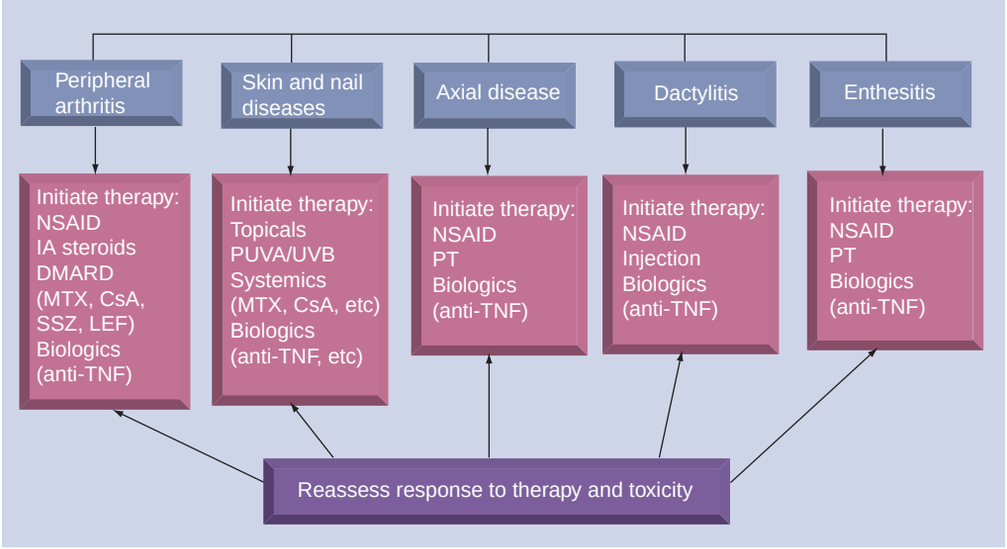

Figure 1. GRAPPA treatment guidelines for psoriatic arthritis, categorized by disease characteristics and distinct organ involvement. CsA: Ciclosporin A; GRAPPA: Group of Research and Assessment of Psoriasis and Psoriatic Arthritis; IA: Intra-articular; LEF: Leflunomide; MTX: Methotrexate; PT: Physiotherapy; PUVA/UVB: PsA psoralen plus ultraviolet; SSZ: Sulfazalasine.
Reproduced with permission from [48].

Box 1. Classification criteria for psoriatic arthritis (CASPAR) criteria.

Inflammatory articular disease (joint, spine or entheseal) plus three points from the following five categories:

- Evidence of psoriasis:
  - Current psoriasis: defined as psoriatic skin or scalp disease present today as judged by a rheumatologist or dermatologist.
  - A personal history of psoriasis: defined as a history of psoriasis that may be obtained from a patient, family physician, dermatologist, rheumatologist or other qualified healthcare provider.
  - A family history of psoriasis is defined as a history of psoriasis in a first- or second-degree relative according to patient report.
- Typical psoriatic nail dystrophy: including onycholysis, pitting and hyperkeratosis observed on current physical examination.
- A negative test result for the presence of rheumatoid factor by any method except latex but preferably by enzyme-linked immunosorbent assay or nephelometry, according to the local laboratory reference range.
- Radiographic evidence of juxta-articular new bone formation, appearing as ill-defined ossification near joint margins (but excluding osteophyte formation) on plain radiographs of the hand or foot.

Current psoriasis is assigned a score of 2; all other features are assigned a score of 1.
Data from [43].

- Acute phase reactants (e.g., C-reactive protein or erythrocyte sedimentation rate);
- Radiographic assessment was encouraged according to clinical manifestation and physician discretionary judgment [37].

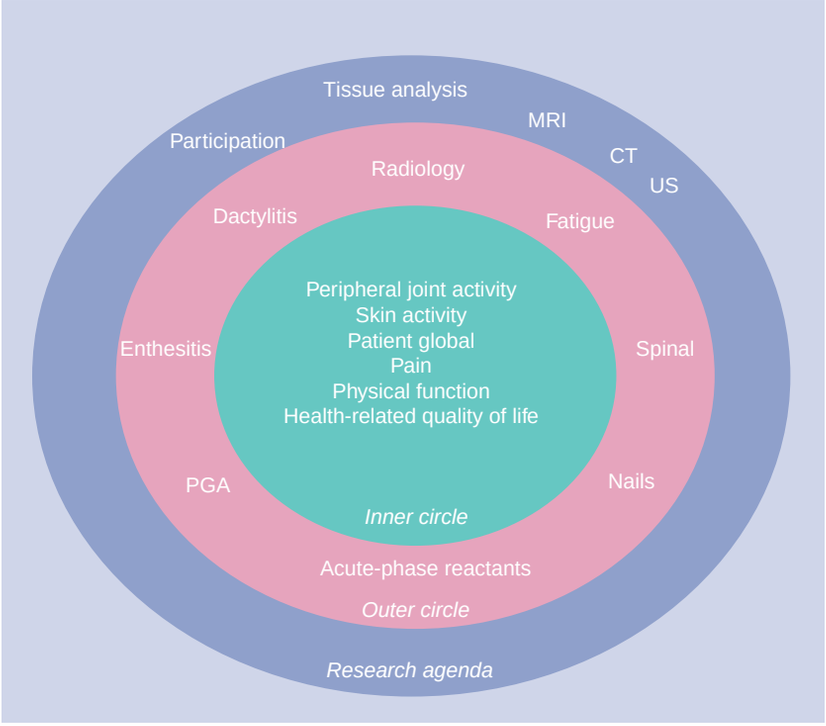

Figure 2. Domains for PsA. Three categories were considered. The items included in the inner core must be included in all RCT and LOS. Other domains recommended but not mandatory are included in the outer core. A set of items requiring further research were put in the research agenda (outer circle).
CT: Computed tomography; LOS: Longitudinal studies; PGA: Physician global assessment; PsA: Psoriatic arthritis; RCT: Randomized controlled trial; US: Ultrasound.
Reproduced with permission from [44].

For response criteria to treatment of peripheral arthritis, GRAPPA recommended tools initially developed for RA, such as the Disease Activity Score 28, as it has shown to be reliable and discriminative in PsA, (even though it uses only 28 joints) and the European League Against Rheumatism response criteria, which categorize levels of disease and changes to assess response [37]. GRAPPA suggested that The American College of Rheumatology response criteria (e.g., ACR20/50/70) may also be used in PsA [37].

Usefulness of clinical guidelines

Clinical guidelines are important instruments to shape evidence-based medicine. Professionals can use guidelines for decision making at the bedside of individual patients. The guidelines may also provide instructions on which diagnostic or screening tests or interventions to be used [45,46].

Clinical practice guidelines are an increasingly common element of clinical care throughout the world. Health systems are investing substantial resources in the development and introduction of clinical guidelines in the belief that they will inform clinical practice promoting effective and cost-effective healthcare. Accordingly clinical guidelines help practitioners to improve their professional practice and the quality of care and patients' outcomes [45,46].

Despite the current interest in guidelines, there remains uncertainty about the likely effectiveness of guideline dissemination and implementation.

Several reviews indicated that when a guideline can be relatively easily understood the chance is greater that the guideline will be used [46].

In that sense most of the guidelines reviewed here, including the recently published GRAPPA guidelines, are almost straightforward.

Other important issues identified is that groups that develop guidelines should be broadly composed and include all relevant health professionals [46]. This was one of the goals of GRAPPA guidelines and was successfully accomplished.

Although there are still many unknown issues that influence the chances of a guideline to be broadly implemented, it seems that most of the guidelines published so far are heading in the right direction.

Conclusion

Several National and one international guideline on treatment of PsA have been published. Strengths and weakness of each of these guidelines have been summarized in Table 4. These guidelines have several similarities and small differences addressing the fact that treatment of rheumatic conditions is now very much standardized worldwide. Guidelines reviewed here are all evidence based and were developed after a thorough review of the existing literature.

The weaknesses of all these recommendations center primarily on the lack of studies with high levels of evidence. Only the most recent trials with anti-TNF agents provide enough evidence on efficacy, and even more importantly, provide evidence on radiographic progression reduction and QOL improvement. As absence of evidence is not evidence of absence, the experience and opinion of experts in the field are always useful to complete recommendations where no information is available. In that sense, all published guidelines, and special GRAPPA developed ones, were devised including broad panels of experts.

The Canadian and French guidelines targeted not only PsA but spondyloarthritis or ankylosing spondylitis, respectively. In that sense both are very much specific and detailed on axial involvement than in other disease manifestations.

The British guidelines put their focus only on peripheral arthritis, while the ones developed mainly by dermatologists, in spite of providing a very extensive review on manifestations, assessments and treatments available are very unspecific at the time of recommendation.

Table 4. Strengths and weakness of different guidelines.

Guideline	Strengths	Weakness
Canadian Rheumatology Association	Evidence based Recommendation for DMARDs use included	Targeting spondyloarthritis Only included axial and peripheral arthritis involvement
British Society of Rheumatology	Evidence based Criteria for starting therapy, monitoring and assessment of response clearly defined	Targeting only peripheral arthritis Considering only anti-TNF treatment
French Society for Rheumatology	Evidence based Criteria for starting therapy, monitoring and assessment of response clearly defined	Targeting ankylosing spondylitis and psoriatic arthritis. Considering only anti-TNF treatment
Italian Society for Rheumatology	Evidence based Criteria for starting therapy, monitoring and assessment of response clearly defined Axial, peripheral, dactyl and enthesis involvement included	Considering only anti-TNF treatment Skin and nails involvement not included
American Academy of Dermatology	Evidence based Extensive review on diagnostic, involvement and assessment tools Extensive literature review on all treatments available	Specific recommendations only for skin and peripheral arthritis involvement Criteria for starting therapy, monitoring and assessment of response not clearly defined
GRAPPA	Evidence based International experts panel Included all disease manifestations (skin, nails, axial, peripheral, enthesis and dactyl involvements) Criteria for starting therapy, monitoring and assessment of response clearly defined Considered unequal severity of different involvements when recommending treatment Recommendation for DMARDs use included	Weak evidence on some recommendations Severity classification used for different involvements not validated

GRAPPA: Group of research and assessment of psoriasis and psoriatic arthritis; SpA: Spondyloarthritis.

The Italian guidelines are probably one of the more comprehensive and detailed related to assessment, and treatment of different manifestations, although they did not include treatment for skin and nail involvement.

The main advance of the GRAPPA guidelines compared with other national guidelines is that they take into account, in a specific manner, all manifestations of psoriatic disease in patients with PsA, including skin, nail and axial involvement, enthesitis and dactylitis. In front of a PsA patient with one of these clinical features the treating physician or regulatory organization could easily find in those guidelines the best treatment available under the light of the existing evidence. In the GRAPPA guidelines, an effort was made to consider psoriatic disease as a whole and to take into account not only the different systems involved but the different severity of each involvement as well. In order to do that a severity grid was developed (TABLE 3) and examples of how to use it included. One of the weakness of this approach was that this grid has not been validated.

With the continuous development of new treatments for rheumatic conditions, guidelines are very rapidly out of date and need frequent revisions. To accomplish this, these revisions should be a compromise of all investigators and practitioners engaged in the development of clinical guidelines.

Psoriatic arthritis is an important and potentially disabling condition. There remains much work to be done in all aspects of the disease, from explaining pathologic mechanisms to finding the most appropriate treatment. The development and implementation of clinical guidelines is sure to help to improve patient's outcomes, QOL and quality of care.

Future perspective

New more effective and expensive treatments are very likely to be introduced in the treatments of PsA. Costs of healthcare keep rising year after year and represent a big challenge to governments, payers and employers alike [47]. Inappropriate care and overuse of new technologies are some of the explanations for rising costs, and can be reduced through shared decision-making between well-informed physicians and patients. In this context evidence-based clinical guidelines developed with experts and patients input would be of great importance to keep the costs within reasonable values while maintaining or even improving quality of care. The future perspective, in my opinion, is that more comprehensive, sophisticated but easy to understand clinical guidelines directed not only at physicians but also at patients, will be developed in the coming years.

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Executive summary

- Psoriatic arthritis is a frequent chronic, potentially disabling disease.
- Traditional DMARDs have shown little effect and there is no evidence that any of these drugs actually prevented disease progression.
- Anti-TNF agents have shown efficacy on symptoms control and prevention of radiographic progression, but are expensive. Several organizations developed clinical guidelines to standardize their use.
- Most clinical guidelines recommended the use of anti-TNF agents for peripheral arthritis after failure of one or two standard DMARDs.
- For axial predominant disease, all guidelines recommended the use of anti-TNF agents after failure of NSAIDs, without trying conventional DMARDs.
- The Group of Research and Assessment of Psoriasis and Psoriatic Arthritis guidelines include all manifestations of psoriatic disease in patients with psoriatic arthritis, including skin, nail and axial involvement, enthesitis and dactylitis.

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CME Treatment guidelines for psoriatic arthritis

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Activity evaluation: where 1 is strongly disagree and 5 is strongly agree.	1	2	3	4	5
The activity supported the learning objectives.					
The material was organized clearly for learning to occur.					
The content learned from this activity will impact my practice.					
The activity was presented objectively and free of commercial bias.					

1. Which of the following statements about the epidemiology and prognosis of psoriatic arthritis (PsA) is most accurate?

- ☐ **A** The majority of patients with psoriasis develop PsA
- ☐ **B** Half of patients with PsA have spinal or sacroiliac involvement
- ☐ **C** Enthesitis is rare in PsA
- ☐ **D** PsA generally does not progress in the first 3 years after diagnosis

2. Which of the following medications most likely reduces the progression of PsA?

- ☐ **A** Infliximab
- ☐ **B** Methotrexate
- ☐ **C** Leflunomide
- ☐ **D** Sulfasalazine

3. All of the following are recommendations for the treatment of PsA according to the Group of Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) guidelines, *except*:

- ☐ **A** Moderate or severe peripheral PsA should be initially treated with TNF inhibitors
- ☐ **B** Nonsteroidal anti-inflammatory drugs (NSAIDs), physical therapy and injection of the sacroiliac joint are first-line therapy for moderate spinal disease
- ☐ **C** Severe enthesitis may prompt the use of TNF inhibitors
- ☐ **D** All three TNF inhibitors may be used to treat severe skin disease

4. All of the following are elements of the assessment of PsA advocated in the current review, *except*:

- ☐ **A** Health-related quality of life
- ☐ **B** Laboratory testing, such as rheumatoid factor and C-reactive protein
- ☐ **C** Radiographic evidence of degenerative disease
- ☐ **D** Previous treatment failures with disease-modifying antirheumatic drugs (DMARDs)