Outcome Measures in Psoriatic Arthritis

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ABSTRACT. Recent advances in biologic therapies have provided hope for patients with psoriatic arthritis (PsA). However, studies have been hampered by the lack of acceptable and validated outcome measures. This article reviews outcome measures used in the assessment of both skin and joints in PsA, and provides a summary of the Psoriatic Arthritis Workshop during OMERACT 7. A set of domains to be included in the assessment of patients with PsA was derived, and a research agenda was developed. (J Rheumatol 2005;32:2262–9)

Key Indexing Terms:
PSORIATIC ARTHRITIS PSORIASIS
ASSESSMENT INSTRUMENTS OUTCOMES CORE SET

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Introduction and Background

Psoriatic arthritis (PsA) has been defined as an inflammatory arthritis associated with psoriasis (Ps), usually seronegative for rheumatoid factor[1]. In addition to peripheral arthritis that tends to be asymmetric, patients with PsA develop dactylitis, spondyloarthritis, tendonitis, and enthesitis, as well as extraarticular features common to the spondyloarthropathies. PsA has therefore been classified among the HLA-B27-associated spondyloarthropathies. However, it should be noted that less than half of the patients with PsA have spondyloarthritis. While initially thought to be mild and rare, PsA has now been recognized as more common and more severe[2]. Medications used to treat PsA have not provided adequate control of inflammation and have not prevented progression of joint damage[3,4].

Recent advances in biologic therapies have provided hope for patients with PsA[4]. Among the difficulties that arise in reviewing the response to these therapies is the lack of acceptable diagnostic classification criteria for PsA and the lack of widely accepted methods of evaluation of the disease.

The issue of classification is currently being addressed by the CASPAR (ClASsification of Psoriatic ARthritis) group, chaired by Dr. Philip Helliwell of Leeds, England. CASPAR includes rheumatologists from around the world who have been collecting data, according to a standard protocol, on patients with PsA and controls with inflammatory and noninflammatory arthritis. These cases will be analyzed for features that best distinguish patients with PsA, including clinical, laboratory, radiology, and genetic markers. The sensitivity and specificity of currently published classification schemes will be tested in this dataset and compared with the newly derived scheme.

GRAPPA, Group for Research and Assessment of Psoriasis and Psoriatic Arthritis, was founded in 2003. This group evolved from the CASPAR effort to include, in addition to rheumatologists, dermatologists and other investigators. GRAPPA has established the following goals:

•Improve awareness of and communication between experts in PsA and Ps, especially between rheumatologists and dermatologists
•Identify and study key domains of inquiry in PsA and Ps
•Develop updated classification criteria of PsA (through CASPAR)
•Validate and standardize outcome assessment tools in PsA and Ps, for both basic clinical and therapeutic studies
•Improve awareness of and communication between PsA/Ps experts and other interested entities, including patient leagues, regulatory agencies, industry, other physicians, and the public
•Improve educational efforts about PsA and Ps
•Improve the conduct and standardization of clinical registries
•Develop treatment guidelines in an evidenced-based manner

The first goal was addressed at a joint meeting in New York in August 2003, with participants from both disciplines; other meetings followed at the American College of Rheumatology (ACR) in October 2003 and the American Academy of Dermatology in February 2004. Currently, only 2 dermatologists are on the steering committee of GRAPPA, but a major goal of the organization is to increase their numbers to proportional representation.

Review of Assessment Instruments for Joint Disease in Psoriatic Arthritis

As the first step to identifying key domains of inquiry in PsA and Ps, a review of available assessment tools was undertaken[5] and disseminated to members of the CASPAR group in preparation for a Delphi exercise to identify domains of inquiry in PsA. A questionnaire e-mailed to 54 rheumatologist members of CASPAR in January 2003 had 4 components regarding domains of inquiry: symptom relief, disease modification, longitudinal studies, and rehabilitation; and 26 possible domains were included. As a result of the first mailing 32 individuals responded. The process involved controlled feedback: the information collected in the first round was analyzed and the aggregate result was distributed to all participants so they could compare their responses, thus allowing individuals to change their approach on subsequent mailings. The 32 initial responders received 2 further mailings, each time receiving information for the total group. As a result of this exercise the list of domains was reduced to 12, and there was more agreement among participants, although the ranking of each domain did not change[6]. The results of this exercise were discussed at a CASPAR meeting during the European League Against Rheumatism conference in June 2003. It was acknowledged that dermatologists were not yet involved and that their involvement would be critical to fully appreciate and incorporate the clinical and quality of life aspects of the skin disease.

To address these concerns a nominal group process exercise took place during the 2003 GRAPPA meeting in New York. During the meeting, the results of the Delphi exercise were first reviewed. Participants were then divided into 3 groups, each including rheumatologists, dermatologists, patients, and industry partners. As a result of these deliberations, a set of domains was identified for assessment of patients with PsA[7]. For some of the domains, instruments were also identified; for others further work is required (Table 1).

Although widely validated and accepted instruments for the assessment of PsA are lacking, several instruments used in recent clinical trials in PsA successfully distinguished drug-treated from placebo-treated patients[5]. The measures used to assess joint disease include ACR response criteria developed for rheumatoid arthritis (RA)[8], the Psoriatic Arthritis Response Criteria (PsARC), developed by Dan Clegg for the sulfasalazine study in PsA[9], and the Disease Activity Score (DAS) response criteria, also developed for RA[10]. These response measures include assessment of tender and swollen joints and patient- and physician-derived scores.

The ACR20 response criteria require a 20% improvement in both tender and swollen joint counts, and a 20% improvement in 3 of 5 items: patient global assessment (visual analog scale, VAS), physician global assessment (VAS), patient pain score (VAS), Health Assessment Questionnaire (HAQ), and either erythrocyte sedimentation rate or C-reactive protein (CRP). For some PsA studies the joint count was increased to 78 to include distal interphalangeal (DIP) joints of the feet. To achieve an ACR50 or ACR70 response, the same guidelines apply but the level of response is 50% or 70% improvement, respectively.

The PsARC include tender joint count, swollen joint count, physician global assessment (0–5 point scale), and patient global assessment (0–5 point scale). A response in the joint count is determined by a reduction of ≥ 30%, whereas a response in the Likert scale is determined by a reduction by 1 score. Overall response is indicated by improvement in 2 of 4 items, one of which must be a joint count. There must not be worsening in any of the 4 items. In some studies using PsARC the joint count was increased to 78, while in others the 68-joint count was used.

Each of the above instruments was used as either a primary or secondary response measure in all of the recent randomized trials in PsA (Table 2). The placebo response in these trials was low for both the ACR20 and the PsARC[11–15]. In anti-tumor necrosis factor (TNF) trials, patients demonstrated high response rates using both instru-

Table 1. Domains for PsA — results from the GRAPPA New York Conference.

Item	Domain	Instrument
Joint inflammation	Peripheral joints	ACR joint count, PsARC (68 or 76) joints, DAS
	Axial skeleton	ND
	Physician global	10 cm VAS
Other features of PsA	Dactylitis	ND
	Enthesitis	Mander, Mases, others ND
Skin	Skin psoriasis extent	ND
	Individual lesion	ND
	Nails	ND
Imaging (damage)	Hands, feet, pelvis	Radiography Other modalities including MRI, US to be investigated
Biomarkers	CRP, ESR	Cytokines, tissue (skin, synovium) and other biomarkers to be investigated
Patient-derived	Patient global	10 cm VAS
	Pain	10 cm VAS
	Quality of life related to joint and skin disease	SF-36, DLQI, PsAQoL, other
	Itching	ND
	Function	HAQ
	Fatigue	Krupp, FACIT, MFI, others

ACR: American College of Rheumatology; ND: not determined; PsARC: Psoriatic Arthritis Response Criteria; DAS: Disease Activity Score; Mander: 66 enthesitis sites; Mases: Ankylosing Spondylitis Assessment group enthesitis count (13 sites); MRI: magnetic resonance imaging; US: ultrasound; DLQI: Dermatology Life Quality Index; PsAQoL: Psoriatic Arthritis Quality of Life instrument; HAQ: Health Assessment Questionnaire; Krupp: Krupp Fatigue Scale; FACIT: Functional Assessment Chronic Illness Therapy; MFI: multidimensional fatigue inventory. Items ND or investigated were recommended for further research.

Table 2. Articular outcome measures used in PsA clinical trials. All outcome measure values are percentages.

Medication	No. of Patients	Duration, Weeks	Primary Outcome	PsARC		ACR 20		ACR 50		ACR 70	
				Rx	Placebo	Rx	Placebo	Rx	Placebo	Rx	Placebo
Leflunomide[15]	190	24	PsARC	59	29	38.5	20	NA	NA	NA	NA
Etanercept 2[11]	60	12	PsARC	87	23	73	13	50	3	13	0
Etanercept 3[12]	205	12	ACR20	72	31	59	15	38	4	11	0
Etanercept 3[12]	205	24	ACR20	70	24	50	13	37	4	9	1
Etanercept 3[12]	205	48	ACR20	NA	NA	59	57*	38	36*	20	10*
Infliximab[13]	101	16	ACR20	76.5	18	69	8	49	0	29	0
Infliximab[14]	88	52	ACR20	NA	NA	72	77*	54	49*	35	30*

* Responses in the open-labeled component patients originally assigned to placebo.

ments, whether they were used as primary or secondary outcome measures. Initially, there was concern about measuring acute phase reactants, because they are elevated in only about 50% of the patients with PsA[16]. Similarly, HAQ scores tend to be lower in PsA compared to RA patients[17]. The data from the trials, however, indicate that both the CRP and the HAQ score are valid measures, since they both improved significantly in several therapeutic trials[18].

The DAS includes a joint count, which is based on the Ritchie index, as well as patient- and physician-derived scores. A score is calculated based on a formula and recorded for each visit. A patient response may be considered good, moderate, or poor (EULAR response criteria) based on the change in DAS scores. Thus, an advantage of the DAS is that it tracks both disease activity and response to change. However, a current limitation is that DIP joints are excluded and inclusion of this criterion requires revalidation. Nonetheless, the DAS and DAS28 (including only 28 joints) were analyzed as secondary outcomes in the Infliximab Multinational Psoriatic Arthritis Trial (IMPACT), and these instruments distinguished infliximab from placebo-treated patients at 16 weeks[13]. However, if used as an entry criterion, the DAS28 would have reduced the number of eligible patients by 25%.

Thus, based on their ability to distinguish between drug-treated and placebo-treated patients, the ACR, PsARC, and EULAR response criteria for outcome assessment in RA appear to be valid in the assessment of peripheral arthritis in PsA.

Measures of enthesitis and dactylitis are in development for use in PsA trials. The assessment of spinal disease has

not been included in clinical trials to date, as there are no acceptable tools. Such measures will require development and validation as well.

Quality of life and measures of function have also been studied in PsA clinical trials. The HAQ, which assesses function related to arthritis, and the Medical Outcome Study Short-form 36 (SF-36), a generic quality of life instrument, have both been validated in PsA[19]. Recent randomized controlled trials with anti-TNF agents and leflunomide in PsA demonstrated significant reductions in HAQ scores[12,13-15]. The SF-36 has also demonstrated significant improvement in recent trials[12]. A new quality of life measure, the PsAQoL, has recently been developed for PsA, and requires further validation in clinical trials[20].

Another important outcome measure in PsA is the assessment of damage, and in particular the ability of medications to prevent or arrest radiological damage[21]. Several attempts to validate radiological assessment tools in PsA have recently been published. Rahman, *et al*[22] reported that the Steinbrocker method of assessing peripheral joint damage, which assigns the worst joint grade on a 0 to 4 scale as the patient's grade, yields good inter- and intra-rater reliability, but is not sensitive to change. However, a modification of that method, which assigns a grade to each joint on the same scale, demonstrated both intra- and inter-observer reliability and sensitivity to change, as did the Larsen method. Wassenberg, *et al*[23] developed a system that incorporates both the assessment of peripheral joint disease and specific radiological manifestations in PsA. This system, called the PsA Ratingen score, has not been tested in drug trials. The Sharp scoring system[24] modified to include the DIP joints was tested in a randomized controlled trial of etanercept in PsA, and demonstrated the ability of etanercept to prevent progression of erosions in PsA[12]. This study included only radiographs of the hands and wrists. The van der Heijde modification of the Sharp scoring system[25] was recently used to identify radiographic changes in the course of the IMPACT study, and the results showed that infliximab may prevent progression of joint damage, although because of the short duration on placebo (16 weeks) the expected progression was computed from baseline values[26]. In the near future, the 4 scoring methods (modified Steinbrocker, PsA Ratingen score, Sharp score, and van der Heijde modified Sharp score) will be compared for reliability and sensitivity to change. The precise characteristics of these scoring methods and the available knowledge on various validity aspects have been reviewed[21].

Review of Assessment Instruments for Skin Disease in Psoriatic Arthritis

Since Ps is a major component of the disease in PsA, it is most important to evaluate skin disease as well as joint manifestations. A number of tools have been developed for the assessment of Ps. Two general approaches govern the endpoints of these assessments: one is subjective and the other is objective. For the subjective endpoints the physician and/or patient is asked if they think there has been improvement or worsening, and to provide a global score — the Physicians or Patients Global Assessment (PGA or PtGA) — that is either dynamic or static. Objective endpoints include photographs, body surface area, and induration (thickness of lesion). Specific tools include the Psoriasis Area Severity Index (PASI)[27], the Lattice System Physician Global Assessment[28], and the National Psoriasis Foundation Psoriasis Score (NPF-PS)[29].

Typically, the dynamic PGA of skin (0–7 scale from clear to severe) is scored relative to baseline values and based on the evaluator's memory, with or without the aid of a picture representing the patient's disease at baseline. Alternatively, the global assessment may be static, describing the disease (percentage of body covered with psoriasis and a scoring of the amount of erythema, scaling, and induration relative to a standardized worded description or to photographic standards) at each session. However, the terms that define the static components have not been standardized across all trials.

PASI was developed in 1978 and was used first in a retinoid study[27]. Basically PASI is a sum of scores for 4 body parts, based on each lesion and assessing erythema, thickness, and scale, and then derived through a fairly complicated formula and expressed as percentage of involvement. The PASI has a range of 0–72 (Table 3). A limitation of the PASI is that induration (thickness), thought to be the most sensitive characteristic by investigator consensus[29,30], is not carefully defined. The area is nonlinear. Erythema, induration, and scale are all weighted equally. Because of its design the top half of the scale is uncommonly used. In recent clinical trials the number of subjects achieving a 75% reduction of PASI score has been the primary endpoint. Many do not achieve this level of clinical improvement, but still have clinically meaningful improvement[30]. Moreover, PASI does not work well when the affected body surface area is below 3%, or the PASI score is less than 2.5%.

Table 3. PASI scoring system.

	Head	Trunk†	Upper Extremity	Lower Extremity
Erythema	0–4*	0–4	0–4	0–4
Induration	0–4	0–4	0–4	0–4
Scale	0–4	0–4	0–4	0–4
Area	0–6**	0–6	0–6	0–6
Factor***	0.1	0.3	0.2	0.3

† Trunk includes axilla and groin; buttocks count included with the lower extremity. * Scored as none = 0, slight = 1, moderate = 2, severe = 3, very severe = 4. ** Area scored as 0 = 0 to < 10% = 1; 10–30% = 2; 30–50% = 3; 50–70% = 4; 70–90% = 5; > 90% = 6. *** Calculated by adding the scores for erythema, induration, and scale in each of the 4 parts of the body, multiplying by the area affected, and then multiplying by the factor assigned to each part. The score ranges from 0 to 72.

Regarding the limitation of the PASI in distinguishing active treatment from placebo, it has recently been recognized that a clinically significant treatment must provide both clinically meaningful improvement and be statistically significant in a properly blinded and powered clinical trial. Additionally, an objective endpoint that measures the clinically meaningful treatment would be useless if it could not differentiate active from placebo. In 3 recent placebo-controlled trials of alefacept, efalizumab, and etanercept, statistical differences from placebo were consistently shown by improvements in PASI (Table 4)[30]. Usually PASI 50 encompasses improvements in PASI from 50% to 100%. For this analysis improvement was separated into 2 components, 50% to < 75% and ≥ 75% reduction in PASI. Improvements in both groups showed significant changes relative to placebo. These analyses also demonstrate that a 50% reduction in PASI will distinguish active disease from placebo (Table 4).

The Lattice System Physicians Global Assessment was developed by Ellis and colleagues[28] to qualitatively assess elements of each plaque, resulting in a global score that ranges over 8 steps, from clear to very severe. There are several steps in completing this scoring system. In step one, the percentage of the body surface involved is identified, followed by determination of the plaque qualities (thickness, erythema, and scale) averaged over the entire body.

Analysis of the PGA, PASI, and the Lattice System showed these instruments to be highly correlated[28]; intra-rater variation was highest for PASI and significantly less for PGA and Lattice. The inter-rater variation similarly was highest for PASI and much less for both the other 2 systems[28].

The National Psoriasis Foundation Psoriasis Score (NPF-PS) is a composite assessment of investigator and patient characteristics developed to answer the US Food and Drug Administration's criticisms of the PASI and to include skin involvement of Ps in a system that uses ACR and PsA response criteria assessment of joint disease[29,31]. This instrument is based on characteristics felt to be most sensitive [thickness of 2 target lesions and change in body surface area (BSA), from baseline] in assessing Ps, and was also created to provide better cross-study comparisons versus the current instruments (Tables 5 and 6). The NPF-PS includes both objective and subjective assessment. It has 6 endpoints. Two representative target lesions are selected, and the thickness of each is assessed relative to set thickness (induration; 0–1.25 mm) on an embossed card. The third element is change in BSA from baseline. There is a PGA and a PtGA as well as an itch assessment. Each of these subjective endpoints carries a definition and thus is a static assessment. Each of the 6 characteristics carries a score of 0 to 5; the maximum score is 30, and "no disease" = 0. For settings where the BSA is relatively small (< 3%) the NPF-PS allows a wider numerical change than the PASI score. PASI measures change in BSA relative to baseline; thus the PASI is not sensitive to BSA; however, sensitivity to BSA is important in trials of PsA, where frequently the area covered with Ps is very small, < 3%.

The PASI was used as an outcome measure in recent randomized controlled trials (RCT) in PsA, where BSA was only calculated in patients who had Ps on a surface area > 3%, or a PASI > 2.5, depending on the study. In those patients, there was a significant response both to anti-TNF agents and to leflunomide among patients with PsA[11-14]. Another outcome measure used to assess the skin in these trials was the assessment of target lesion, i.e., a psoriatic plaque at least 2 cm in diameter, which is evaluated for response in erythema, induration, and scale in a manner similar to the assessment of the PASI score and the NPF-PS. Target lesions demonstrated a statistically significant response in recent RCT in PsA as well (Table 7). The Dermatologists Static Global Assessment of Psoriasis scale has also been used in the etanercept PsA trial[12].

Table 8 provides a summary of the assessment tools to measure response to therapeutic intervention. Those that have been used most widely have been validated, but have limitations, while recently developed instruments may avoid some of the limitations but have not yet been validated. The assessment of nail lesions also requires further development and validation.

Table 4. Percentage of patients receiving active drug versus placebo that achieved improvement in PASI scores of 50 to < 75% and ≥ 75%.

	PASI ≥ 75%		PASI 50 to < 75%	
	Active Tx	Placebo	Active Tx	Placebo
Alefacept* (7.5 mg/wk)	28†	8	28†	16
Efalizumab†† (1.0 mg/kg/wk)	22.4†	4.9	29.3†	15.6
Efalizumab†† (2.0 mg/kg/wk)	28.4†	4.9	28.4†	15.6
Etanercept**	30†	2	40†	9

* Alefacept phase III trial (n = 553); results from the 1st course of alefacept intravenous injections vs placebo in which the greatest overall improvement in PASI that occurred during the 12-week treatment of the 12-week post treatment period was reported. † $p < 0.0001$ vs placebo. †† Efalizumab phase III trial (n = 597); results from the 1st course of efalizumab subcutaneous injections in which improvement in PASI was reported at end of week 12. ** Etanercept phase II trial (n = 112); results from the 1st course of etanercept subcutaneous injections in which improvement in PASI score was reported at the end of week 12.

Table 5. Elements of National Psoriasis Foundation Psoriasis Score (NPF-PS).

	Score
1. Induration of representative target lesion A (0 to ≥ 1.25 mm)	0 to 5
2. Induration of representative target lesion B (0 to ≥ 1.25 mm)	0 to 5
3. Body surface area relative to baseline as a percentage (score is 20% intervals)	0 to 5
4. Physician's global assessment (static and defined)	0 to 5
5. Patient's global assessment (relative to worst the disease has been ever)	0 to 5
6. Patient's assessment of itch (defined score = average over 24 h)	0 to 5
Range of total score	0 to 30

Thus there is a great need to finalize domains and instruments to assess PsA and Ps for both clinical trials and observational cohorts, to further research and validate the instruments that are currently used, and to develop tools to measure other features of the disease.

PsA Workshop at OMERACT 7

The objectives of the PsA workshop:

1. Identify domains for inclusion in clinical trials of PsA.
2. Develop a core set of domains to be used in clinical trials in PsA.
3. Identify instruments to be used for the domains.
4. Develop a research agenda.

The workshop began with a plenary session presentation that reviewed the process of identifying domains in PsA, followed by a review of domains identified through the Delphi and nominal group processes over the previous year. Instruments used in clinical trials in PsA and psoriasis were reviewed in detail, as well as radiographic methods used in PsA. A detailed description of these instruments has been recently published[5]. Following the formal presentations the participants formed breakout groups. Each group ranked items to be included in a clinical trial from 1 to 14 in terms of importance. Each group considered whether to propose adding other worthy items that had not been included. Each group was to identify those items that were absolutely critical for inclusion in a core set.

Table 6. Elements of 4 global assessment scores for psoriasis.

1. Lattice System-Global Psoriasis Score in Rating Psoriasis
   Global score, range = 8 steps (clear to very severe) — step scores
   Plaque qualities defined
   Weights elevation (induration) preferentially
2. Physician's Static Global Assessment
   0 = clear, scores of 1 to 6 increasing severity
   Requires definition of each score
3. Physician's Dynamic Global Assessment
   Usually used as a 7 point score
   0 = clear, scores of 1 to 5 = increasing severity
   6 = worsened
   Requires recall memory or assistance with baseline photograph
4. Overall Lesion Assessment
   5 point scale, 0 = none; 4 = very severe
   Component 1 = thickness score, composite of all lesions

Summary of Discussions at Breakout Groups

Members of GRAPPA acted as scribes for each of 12 groups and reported on the discussions that took place in their groups at a GRAPPA meeting following the breakout session. The following is a summary of those discussions: It was suggested that several items were not domains. Specifically, it was noted that the active joint count is used to assess inflammation and should be replaced with *joint activity*. Similarly, radiology is a method, not a domain, and should be replaced with *structural damage*. Spinal mobility is a measure used to assess axial involvement and should be replaced with *axial involvement*. Whether there should be 3 core sets — one for skin, one for peripheral joints, and one for axial disease — or one core set for psoriasis and arthritis was raised as an issue. Other questions included whether peripheral joints should be looked at separately from axial involvement, since different tools would be used for assessment of each component of arthritis; and whether all patients with PsA should be assessed for axial involvement. Discussion suggested there are different instruments to measure peripheral joint activity and spinal involvement,

Table 7. PASI scores in randomized clinical trials in PsA.

Medication	No. of Patients	Duration, weeks	PASI % Reduction Rx	PASI % Reduction Placebo	PASI > 75% Rx	PASI > 75% Placebo
Leflunomide[15]	190	24	23.8	0	NA	NA
Etanercept 2[11]	60	12	46	9	NA	NA
Etanercept 3[12]	128	12	38	3	NA	NA
Etanercept 3[12]	128	24	42	8	23	3
Etanercept 3[12]	91	48	NA	NA	38.5	NA
Infliximab[13]	101	16	81	–35	67	0
Infliximab[14]	88	52	81	73	67	50

Table 8. Ranking based on breakout group voting.

Domain	Rank
Joint activity	1
Patient global	2
Pain	3
Physical function	4
Structural damage	5
Skin disease	6
Quality of life	7
Enthesitis	8
Physician global	9
Acute phase reactants	10
Dactylitis	11
Axial involvement	12
Morning stiffness	13
Damaged joint count	14

but that patients with PsA should be assessed for spinal involvement. Another issue was how many peripheral joints should be counted — 76 joints, 68 joints, 44 joints, or 28 joints, which is a question of parsimony versus comprehensiveness. Generally, a larger number was considered better, since 44 and 28-joint counts excluded feet and distal joints that are commonly affected in PsA. Inclusion of imaging to assess inflammation was also recommended. A point of contention was whether dactylitis and enthesitis should be combined to avoid double counting of inflamed areas, particularly with regard to dactylitis, where joints of the involved digit would be included in the joint count. However, it was noted that these represented 2 different aspects of disease and that each should be considered. Some individuals did not understand the meaning of clinically damaged joint count, which includes deformities, flail joints, ankylosed joints, and surgery. Another point of debate was how the patient global assessment would reflect both skin and joint disease. It was suggested that in addition to the global question there would be subquestions on skin and joint disease. Several members felt that fatigue and sleep should be added. The issue of tissue assessment was also raised.

Results of Discussion of Breakout Groups and Initial Ranking of Domains

The ranking of different domains from 1 to 14, based on results of voting in the breakout groups, is presented in Table 8. Christian Antoni then presented data from a study that evaluated response of PsA patients to etanercept and from the IMPACT trial[11,13] indicating that ACR20, PsARC, and DAS all functioned well in discriminating between drug and placebo treated patients. These data support the use of response criteria in future trials in patients with PsA. They also further demonstrated that CRP was not a good outcome measure in PsA.

Final Proposal for Domains in PsA

At a plenary session on May 16, 2004, the PsA workshop was summarized and discussed prior to final voting to rank domains for inclusion in PsA clinical trials. During discussions a new domain term, "participation" — the ability of patients to participate in work and leisure activities — was proposed and added to the list of domains for final voting. Results of the final vote are presented in Table 9. It was recommended that the first 11 domains be included in a core set, but that further research be carried out on the remaining items for possible inclusion.

Based on the final vote, a research agenda was also proposed (Table 10). This agenda has now been approved by GRAPPA members and will be undertaken to determine which instruments should be used in the assessment of the identified domains and whether the additional domains should be included in clinical trials in PsA.

Table 9. Results of the vote on domains to be included in clinical trials in PsA.

No.	Item	Score, %
1	Joint activity	99
2	Patient global	96
	All 3 components	76
3	Pain assessment	94
4	Physical function	91
5	Skin disease	86
6	Quality of life	78
7	Structural damage	66
8	Acute phase reactant	64
9	Axial involvement	61
10	Participation	61
11	Enthesitis	60
12	Fatigue	48
13	Dactylitis	48
14	Physician global	41
15	Tissue histology	38
16	MRI	34
17	Morning stiffness	25
18	Damage joint count	20

Table 10. Proposed research agenda for PsA.

- Identify optimal joint count
- Develop instrument for patient global assessment to incorporate skin and joint question
- Identify optimal skin assessment
- Develop tools to define structural damage
- Develop instruments for axial assessment
- Develop a tool for the assessment of participation
- Develop instruments for the assessment of enthesitis
- Develop tools for the assessment of dactylitis
- Imaging modalities to assess inflammation and damage
- Develop composite responder indices
- Differential tissue response to therapies
- Study methods to evaluate fatigue in PsA

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