

# Associations between five important domains of health and the Patient Acceptable Symptom State in rheumatoid arthritis and psoriatic arthritis: A cross sectional study of 977 patients

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### Running head: PASS in RA and PsA

Associations between five important domains of health and the Patient Acceptable Symptom State in rheumatoid arthritis and psoriatic arthritis: a cross sectional study of 977 patients.

**Authors**: Déborah Puyraimond-Zemmour, MD <sup>1</sup>, Adrien Etcheto, MSc <sup>2</sup>, Bruno Fautrel , MD, PhD <sup>1</sup>, Andra Balanescu, MD <sup>3</sup> , Maarten de Wit, PhD <sup>4</sup>, Turid Heiberg, RN, PhD <sup>5</sup>, Kati Otsa, MD <sup>6</sup>, Tore K. Kvien, MD <sup>7</sup>, Maxime Dougados, MD <sup>2</sup>, Laure Gossec, MD, PhD <sup>1</sup>.

### Affiliations:

- 1: Sorbonne University, UPMC University Paris 06, Institut Pierre Louis d'Epidémiologie et de Santé Publique, GRC-UPMC 08 (EEMOIS); AP-HP, Pitié Salpêtrière Hospital, Department of rheumatology, Paris, France
- 2: Paris Descartes University, Rheumatology Department, Cochin Hospital, AP-HP; INSERM (U1153): Clinical Epidemiology and Biostatistics, PRES Sorbonne Paris-Cité, Paris, France.
- 3: Research Center of Rheumatic Diseases, "Sf. Maria" Hospital, University of Medicine and Pharmacy "Carol Davila", Bucharest Romania
- 4: EULAR standing committee of People with Arthritis/Rheumatism in Europe (PARE), Zurich, Switzerland
- 5: Østfold University College, Halden, Norway
- 6: Rheumatology Department, Tallinn Central Hospital, Estonia
- 7: Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway

**Corresponding author**: Pr. Laure Gossec, Hôpital Pitié-Salpêtrière, Service de Rhumatologie, 47-83, boulevard de l'Hôpital - 75013 Paris France

laure.gossec@aphp.fr Tel: +33 1 42 17 84 21 Fax: +33 1 42 17 79 59

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### **Abstract (247 words)**

**Introduction:** The objective was to explore the link between a patient acceptable symptom state (PASS) and patient-perceived impact in rheumatoid arthritis (RA) and psoriatic arthritis (PsA).

Patients and Methods: Cross-sectional study of unselected patients with definite RA or PsA. Pain, functional capacity, fatigue, coping and sleep disturbance were assessed by a numeric rating scale (0-10) and compared between patients in PASS or not (Cohen's effect sizes). The domains of health associated with PASS status were assessed by multivariate forward logistic regression, and PASS thresholds were determined using the 75<sup>th</sup> percentile method and ROC analyses.

**Results:** Among 977 patients (531 RA, 446 PsA) mean age was 53.4±13.2 yrs; mean disease duration was 11.2±10.0 yrs; 637 (65.8%) were females. In all, 595 patients (60.9%) were in PASS: they had lower symptom levels, and all domains of health except sleep disturbance discriminated clearly between patients in PASS or not (effect sizes, 0.73 to 1.45 in RA and 0.82 to 1.52 in PsA). In multivariate analysis, less pain and better coping were predictive of being in PASS: odds ratio [95% confidence interval] 0.80 [0.67-0.96] and 0.63 [0.52-0.75] for pain and 0.84 [0.74-0.96] and 0.83 [0.71-0.97] for coping, in RA and PsA respectively. The cutoffs of symptom intensity (range 0-10) corresponding to PASS for the five domains of health and the two diseases were similar, i.e. around 4-5.

### Conclusion:

In RA and PsA, PASS was associated with the five domains of health analysed, and in particular with less pain and better coping.

## **Significance and Innovations**

- 1. Two thirds of 977 unselected tertiary care patients with rheumatoid arthritis (RA) or psoriatic arthritis (PsA) were in patient acceptable symptom state (PASS).
- 2. As expected, patients in PASS had less pain and fatigue and greater functional capacity and coping. Sleep disturbance was not discriminative for PASS status. In multivariate analysis, lower pain and better coping were associated with PASS in RA and PsA.
- 3. PASS levels in the two diseases for pain, functional capacity, coping, fatigue and sleep disturbance as well as the RAID and PsAID scores were similar with cut-offs around 4-5 points (0-10 scale).

The objectives of treatments in rheumatoid arthritis (RA) and psoriatic arthritis (PsA) include acceptable quality of life from the patient's perspective. One simple question can be used to evaluate the level of acceptability of the disease status by a patient: the patient acceptable symptom state (PASS) which corresponds to the concept of "feeling well".[1-5] The PASS is assessed by the question "If you were to remain for the next few months as you were during the last week, would this be acceptable or unacceptable to you?". The PASS appears only weakly related to objective disease activity: in RA, PASS seems to be in the range of moderate disease activity and not remission.[1, 2, 5] Little is known about this relationship in PsA.

It is currently unclear what drives a PASS in a given patient. Since disease activity does not appear to be the main driver, patient-perceived impact is probably more closely related to PASS. RA and PsA are both chronic diseases and impact the patient mainly by 5 domains classified in three categories: physically through pain, functional capacity and sleep disturbance, mentally through coping and mixed (mentally and physically) through fatigue.[6-11] We recently showed that five domains of health are selected by patients with both RA and PsA, as important for overall disease impact: these domains are pain, functional capacity, fatigue, sleep disturbance and coping.[10, 12, 13] Coping can be defined as an adjustment strategy to disease.[14, 15] We asked ourselves which of these symptoms predominantly explain the PASS. Furthermore, the levels of symptoms corresponding to a PASS may be different across domains of health. It is known that pain levels around 4 (on a 0-10 scale) correspond to PASS in different diseases but the PASS level for other domains of health is unknown.[5]

The objective of the present study was to explore the relationships between five domains of health (pain, functional capacity, fatigue, sleep disorders and coping) and PASS in RA and PsA.

### Materials and methods

### Study design and patients

The present study was a post hoc analysis of two international cross-sectional, multicenter studies, involving for RA 10 European countries and for PsA 13 European countries.[12, 13] All the patients included had a definite diagnosis of either RA or PsA according to the physician. The present analyses concerned only patients who had answered the PASS question.

### PASS and symptoms

The PASS was assessed as a binary answer to the following question: "If you were to remain for the next few months as you were during the last week, would this be acceptable or unacceptable to you?".[1, 2, 5]

Five domains of health were analysed: pain, functional capacity, fatigue, sleep disturbance and coping. They were assessed in both diseases by a numeric rating scale (0-10); 0 corresponds to the best state and 10 to the worst. The questions used were phrased similarly in both diseases, and are issued from the RA impact of disease (RAID) and PsA impact of disease (PsAID12) questionnaires.

RAID and PsAID are new composite response scores for RA and PsA.[12, 13, 16] They reflect the impact of the disease on domains of health and are based on the patient's perspective. Seven domains of health are included in RAID and 9 in PsAID. The 5 that are in common were analysed here, to compare the impact of domains of health of RA and PsA. Each domain is assessed through a single question answered by a 0 to 10 numerical rating scale (0 corresponds to the best state and 10 to the worst). The questions used for each domain of health are: "Please tell us how you have been feeling this last week. Circle the number that best describes (your pain/ your fatigue/ your difficulty you had in doing daily physical activities/ your sleep difficulties/ how well did you cope) during the last

### Other data collection

Other data collected included patients' gender and age, characteristics of the disease: duration, swollen joint count (0-28), tender joint count (0-28) and Disease Activity Score based on erythrocyte sedimentation rate (DAS28-ESR). Patients were divided into two groups according to their disease activity: inferior or equal to 3.2 for patients in clinical remission and low disease activity, and superior to 3.2 for patients with moderate or high activity.[17] The Health Assessment Questionnaire (HAQ, range 0-3) and treatments (current synthetic or biologic disease modifying anti-rheumatic drugs (csDMARDs or bDMARDs), current oral glucocorticoids) were also collected.[18]

### Statistical analysis

Mean levels of symptoms for patients in PASS or not in PASS were compared in both diseases, using parametric tests and Cohen's effect size.[19] Cohen's *d* indicates the standardised difference between two means and is usually considered relevant if > 0.5. The associations between the five domains of health and PASS were assessed by multivariate forward logistic regression, after including domains with p<0.20 in the univariate logistic regression. Although there was some colinearity between the outcomes and the DAS28-ESR the logistic regression was adjusted on DAS28-ESR categories. In this multivariate analysis, 188 patients were not analyzed due to missing data (12.6% in RA and 27.1% in PsA). Sensitivity analyses were then performed without adjusting on DAS, and omitting coping.

Thresholds of levels of symptoms and of the RAID and PsAID total scores corresponding to a PASS status were determined for each domain of health and for each disease, using both the 75<sup>th</sup> percentile method (the PASS cut-offs were defined as the 75<sup>th</sup> percentile of the final score in patients who considered their state acceptable) and Receiver-Operating Characteristics (ROC) curve

analyses.[5, 12, 13] Then, sensitivities and specificities of these thresholds by the 75<sup>th</sup> percentile method were calculated against being in PASS or not, as the gold standard. Analyses were performed using SAS version 9.2.

### Results

In all, 977 patients were analyzed (Table 1): 531 with RA and 446 with PsA; mean age was 53.4±13.2 yrs; 637 (65.8%) were females. Most had long-standing disease (mean disease duration, 11.2±10.0 yrs); 359 (38.6%) patients were taking bDMARDs. For PsA patients, current skin psoriasis with body surface>5% concerned 18.8% of the patients. Disease activity was moderate: 348 patients (44.1% with data available) were in remission or low disease activity according to DAS28-ESR. However, symptoms remained high e.g. mean pain (0-10) was 4.7± 2.8 and mean patient global assessment was 4.2 ± 2.6 (Table 1).

### Prevalence of PASS

In all, 595 patients (60.9%) considered themselves in PASS. The percentage in both groups were almost similar: 274 (60.4%) in RA versus 321 (61.4%) in PsA (p=0.80).

### Symptoms and PASS

Patients in PASS had lower levels of symptoms (Table 2): the five domains of impact all discriminated well patients in PASS versus not (effect sizes, 0.73 to 1.45 in RA and 0.82 to 1.52 in PsA). The lowest discriminance was observed for sleep (effect size 0.73 and 0.82 in RA and PsA respectively).

The multivariate analyses were performed on patients with full data. The main missing information was DAS28: RA patients with missing DAS28 had higher symptom levels than those with full information, PsA patients with or without

missing data were similar (data not shown). In multivariate analyses of the five domains of health, only pain and coping were associated with being in PASS, after adjustment on DAS28: the odds ratio [95% confidence interval] were for pain 0.80 [0.67-0.96] in RA and 0.63 [0.52-0.75] in PsA and for coping 0.84 [0.74-0.96] in RA and 0.83 [0.71-0.97] in PsA. Sensitivity analyses with and without adjustement on DAS confirmed the results (data not shown). Furthermore, the sensitivity analysis without coping confirmed the link between pain and PASS in both diseases (results not shown).

### **Thresholds**

Thresholds corresponding to PASS levels for the five domains and the two diseases were similar (Table 3). In both diseases, symptom levels around 4 to 5 points or less (on a 0-10 scale) were best related to PASS status. Sensitivities ranged from 0.75 to 0.84 and specificities from 0.44 to 0.77 with the lowest specificity for sleep (0.44 in RA, 0.50 in PsA) and the highest for pain (0.73 in RA and 0.77 in PsA) (Table 3).[5] A RAID score value of 4.67 and a PsAID score value of 3.75 corresponded to PASS (Table 3).

### **Discussion**

The present study brings important information on PASS in RA and PsA. Two thirds of patients were in PASS status in this unselected tertiary care center study and patients in PASS had better health status for all domains of health though sleep was the least discriminant domain. In multivariate analyses, low pain and high coping levels appeared to be the main drivers of PASS in both diseases.

PASS levels for the five domains and the two diseases were similar with cut-offs around 4-5 points (on a 0-10 scale).

This study has some limitations. Although the sample size was large, these results have to be interpreted taking into account the heterogeneity of the two populations from countries with differing characteristics of several disease and treatments.[12,13] However, this heterogeneity may also reinforce the external validity of the present study. Another limit of this study is the missing data for DAS28 (19.2% overall) which may have consequences on the results of the multivariate analyses, as almost one third of the PsA population (27%) was not included in this analysis. However a sensitivity analysis on all patients confirmed the main results. Furthermore patients with missing data appeared to have higher symptom levels (data not shown). Moreover, only 5 domains of health were analysed here, whereas probably other domains such as psychological distress 10

could be important.[20,22] However, the five domains chosen in the present study were selected by patients as reflecting impact of disease, and were common to both diseases which allowed comparisons.[10,12,13] However, the single questions used here to evaluate the impact of disease may be understood differently. The interpretation of the questions and their representation by patients may affect the reliability of the assessment of a particular domain.

In PsA and RA, the percentage of patients considering themselves in PASS was similar (around 60-70%) and the value seems similar in the published literature.[3-5] It is surprising that although disease activity was different in RA and PsA (as assessed by DAS28-ESR), symptom levels and PASS were similar. This may suggest either (a) that DAS28 did not correctly assess disease activity in particular in PsA, (b) that patients score symptoms independently from disease activity or (c) that DAS28 did not reflect well enough the patients' opinion, in particular in PsA.[23,24] Of note, HAQ seemed better associated with PASS, probably because the questions concerned activities of everyday life, confirming that patient-reported outcomes are often associated.[25]

The definition of the PASS is anchored in the personal experience of the patient (satisfaction and adaptation to symptoms). In this study, pain was the major domain to explain PASS status; pain is regularly reported as essential by people with RA and PsA.[8, 9, 11, 12, 13] Coping seemed to be the second important domain of health associated with PASS in RA. In a previous study, the optimal predictors of pain in RA were physical disability and passive coping, which accounted for 40% of the variance associated with pain.[15] There are no such data for PsA. Moreover, this study confirms the theory of an "impact triad" as proposed by Sanderson et al.: the impact of disease is more than symptom severity, it also includes self-management (coping) and symptom importance.[30]

Sleep disturbance did not discriminate well between patients in PASS or not which could be explained by the multifactorial nature of sleep disorders, and the indirect effect of these disorders on other symptoms, in particular pain and fatigue.[26]

In this study, the PASS cut-offs for the five domains and the two diseases were around 4 to 5 on scales with a range from 0 to 10, which was in agreement with the results of previous studies. In RA, PASS threshold for pain was 4.[5] Of note there were no previous data for the other outcomes and no data in PsA. Thus we believe this brings important and original results.

These results indicate an interesting stability of levels acceptable to a patient, although the domains of health are very different, some being more physical and some more psychological, and although the 2 diseases assessed here are also very different. This consistency across diseases and domains can be considered as a strength of the PASS.

Taking into account how the PASS reflects patient-perceived impact of disease, levels of symptoms corresponding to a PASS might be considered as a clinically relevant treatment target.[27-28] However, in these chronic, erosive diseases, the ultimate objectives of management are not only quality of life, but also halting or reducing the disease progression.[24, 29] In this regard, patient-reported outcomes overall, and in particular both PASS and levels of symptoms, lack predictive value for later evolution of structural damage or other 'hard' outcomes.[25] The present study could not give more information on this point.

In conclusion, as more knowledge becomes available on PASS but also on patientreported outcomes, it will be interesting to determine if PASS itself or levels of symptoms corresponding to a PASS, as determined here, may be valuable as treatment objectives.

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