

## PROTOCOL

---

### Sleep quality in patients with Psoriatic Arthritis

**Authors:** Peter Benzin, Marie Skougaard, Zara Rebecca Stisen, Tanja Schjødt Jørgensen, Rebekka Lund Hansen, Lourdes M. Perez-Chada, Mette Mogensen, Joseph F. Merola, Lars Erik Kristensen

**Funding:** This study is initiated by the Parker Institute, Copenhagen University Hospital Bispebjerg and Frederiksberg, Frederiksberg Denmark. The study is funded by the Oak Foundation

---

### INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory disease involving joints, skin, entheses, nails, and/or other connective tissues, which might be looked upon as clinical manifestations to be included in the common assessment of disease activity. Though in recent years, it has become apparent that also patient-reported outcome like sleep quality have a huge impact on PsA patients' well-being and quality of life. Sleep quality has been defined as "*Being able to have a restful sleep*", and due to the importance to PsA patients, it has been deemed as a domain where further research is needed (3, 4).

Previous studies assessing sleep quality in a PsA population showed a prevalence ranging from 44.5%-84% (2, 5) and studies including patients with psoriasis (PsO) indicate that poorer quality of sleep is linked to concomitant PsA (6, 7). Sleep disturbances are also common in the general population, though in comparison with prevalence ranging from 10% - 30% (8).

Uncertainty persists when having to explain the effect of PsA on quality of sleep, or vice versa. It has been suggested that sleep disturbances might be part of a vicious circle amplifying both PsA clinical manifestations, fatigue, and quality of sleep (9). Investigating associations between the presence of sleep disturbances and PsA related symptoms has resulted in various outcome associating sleep disturbances to pain, anxiety, enthesitis, levels of c-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), fatigue, inflamed joints, female gender, obesity, psoriasis severity etc. (5, 6, 10). Though, the causal effect of PsA on sleep quality remains unclear.

The primary objective of this study is to examine the prevalence of impaired sleep quality in a Danish PsA cohort compared to patients suffering from psoriasis and healthy controls. Secondary objectives include 1) to assess associations between poor quality of sleep and clinical, laboratory, and patient-reported outcome, and 2) to assess the effect of treatment.

This confidential document is the property of The Parker Institute, Bispebjerg and Frederiksberg Hospitals, Nordre Fasanvej 57, road 8, entrance 19, 2000, Frederiksberg, tlf: +45 38 16 41 58, mail: [parker.frederiksberg@regionh.dk](mailto:parker.frederiksberg@regionh.dk).

No unpublished information contained herein may be disclosed without prior written approval from The Parker Institute. Access to this document must be restricted to relevant parties.

## **STUDY DESIGN AND METHODOLOGY**

The study is designed as a cross-sectional study including PsA patients from the PIPA cohort (11), patients with cutaneous psoriasis without suffering from arthritis recruited from the Department of Dermatology, Bispebjerg Hospital, and healthy controls. Before initiation of the study (22.07.2019) a search was performed in PubMed to investigate available literature regarding the theme: (psoriatic arthritis) AND ((sleep disturbance) OR (sleep disorder) OR (quality of sleep)).

### **Participants**

Patients included in the PIPA cohort are: age  $\geq 18$  years, diagnosed with PsA fulfilling the CASPAR classification criteria, and initiation/switching treatment with either IL17 inhibitor, TNF $\alpha$  inhibitor, or Methotrexate. Healthy controls will be matched with regards to age and gender. There are no additional inclusion or exclusion criteria regarding the present study.

### **Patient perspective**

Informed consent will be obtained. The input will be integrated in the current protocol and data presentation.

### **Setting**

From February 2018 all PsA patients attending their PIPA cohort visits at the Parker Institute, Frederiksberg Hospital, Denmark, have answered the paper-version questionnaires: Pittsburgh Sleep Quality Index (PSQI) (8) (12). A standard PIPA cohort visit includes both clinical interview and examination performed by a physician, ultrasonography of joints and entheses, and standard biochemical analysis for monitoring of PsA disease activity. Interview, examinations, blood sampling, and filling in questionnaires are within the same day.

### **Data retrieval**

To conduct the cross-sectional analysis of sleep quality in PsA, data will be retrieved from all patients having filled in the PSQI and have a total score calculated. Data will be included from the visit that is the first time PSQI appears with a total score. To conduct the follow up investigation of effect of treatment, data will be retrieved from the baseline visit (prior to initiating treatment) and the 4 months follow up visit.

### **Variables and outcome measures**

The PSQI is a 19-item questionnaire used to assess self-reported sleep. The 19 questions are rated in a 7-component score: 1) sleep quality, 2) sleep latency, 3) sleep duration, 4) habitual sleep efficiency, 5) sleep

This confidential document is the property of The Parker Institute, Bispebjerg and Frederiksberg Hospitals, Nordre Fasanvej 57, road 8, entrance 19, 2000, Frederiksberg, tlf: +45 38 16 41 58, mail: [parker.frederiksberg@regionh.dk](mailto:parker.frederiksberg@regionh.dk).

No unpublished information contained herein may be disclosed without prior written approval from The Parker Institute. Access to this document must be restricted to relevant parties.

disturbances 6) use of sleeping medication, and 7) daytime dysfunction. Each component rating from 0 – 3, resulting in global score ranging from 0 to 21. Higher scores indicate worse quality of sleep. Global score of  $\leq 5$  is associated with good quality of sleep whereas global score  $> 5$  is associated with poor quality of sleep (8) (12).

Ancillary variables collected include: 1) physician interview and examination: age, gender, disease duration, swollen and tender joint count (66/68 joint count) and Psoriasis Area Severity Index (PASI), 2) patient-reported outcome: Visual Analogue Scale (global, pain, fatigue), Health Assessment Questionnaire (HAQ), Psoriatic Arthritis Impact of Disease (PsAID), Charlson Comorbidity Index (CCI)

Primary outcome: Prevalence of PsA patients suffering from poor quality of sleep defined by PSQI score  $>5$

Secondary outcome(s):

- 1) Differences in PSQI scores comparing PsA patients, PsO patients and healthy controls
- 2) Correlation between PSQI scores and clinical outcome (DAS28CRP and PASI) and patient-reported outcome (VAS global, pain and fatigue, HAQ and CCI)
- 3) Correlation coefficients when stratifying PsA patients by “good sleepers” (PSQI  $\leq 5$ ) and “poor sleepers” (PSQI  $> 5$ )
- 4) Illustrating the transition of PsA patients’ quality of sleep after 4 months

## DATA ANALYSIS AND STATISTICAL ANALYSIS PLAN

Baseline characteristics are given as medians with interquartile ranges (IQRs) and numbers with corresponding percentages. A nonparametric Kruskal-Wallis test was used to compare the PsA, PsO and healthy controls groups and a  $\chi^2$ -test for the assessment of statistically significant differences in baseline characteristics for continuous and categorical data. Sub-analysis will be conducted to assess differences between PsA patients stratifying by “good sleepers (PSQI  $\leq 5$ ) and “poor sleepers” (PSQI  $> 5$ ), and a Mann-Whitney U test was used for comparative analysis of good sleepers versus bad sleepers. Two-sided p-values  $< 0.05$  are considered as statistically significant.

Results will be presented with **Table 1**. Patient characteristics in PsA patients, PsO patients and healthy controls, **Table 2**. Baseline PsA characteristics stratified by “good sleeper” and “poor sleeper” and **Figure 1**. Transition of patients’ quality of sleep from good to poor sleepers and vice versa.

## ETHICAL CONSIDERATIONS

In accordance with Danish law, the collection of data has been approved by the Ethics Committee of the Capital Region of Denmark and meets GDPR requirements approved by the Capital Region of Denmark. All patients have provided written informed consent to participate. Results whether positive, negative, or inconclusive will be published in relevant international peer-reviewed scientific journals.

## REFERENCES

1. Husni ME, Merola JF, Davin S, editors. The psychosocial burden of psoriatic arthritis. Seminars in arthritis and rheumatism; 2017: Elsevier.
2. Duvetorp A, Østergaard M, Skov L, Seifert O, Tveit K, Danielsen K, et al. Quality of life and contact with healthcare systems among patients with psoriasis and psoriatic arthritis: results from the NORdic PATient survey of Psoriasis and Psoriatic arthritis (NORPAPP). Archives of dermatological research. 2019;311(5):351-60.
3. Orbai A-M, De Wit M, Mease P, Shea JA, Gossec L, Leung YY, et al. International patient and physician consensus on a psoriatic arthritis core outcome set for clinical trials. Annals of the rheumatic diseases. 2017;76(4):673-80.
4. Orbai A-M, De Wit M, Mease PJ, Duffin KC, Elmamoun M, Tillett W, et al. Updating the Psoriatic Arthritis (PsA) core domain set: a report from the PsA workshop at OMERACT 2016. The Journal of rheumatology. 2017;44(10):1522-8.
5. Wong IT, Chandran V, Li S, Gladman DD. Sleep disturbance in psoriatic disease: prevalence and associated factors. The Journal of rheumatology. 2017;44(9):1369-74.
6. Smith MP, Ly K, Thibodeaux Q, Weerasinghe T, Beck K, Shankle L, et al. Factors Influencing Sleep Difficulty and Sleep Quantity in the Citizen Pscientist Psoriatic Cohort. Dermatology and therapy. 2019:1-13.
7. Duffin KC, Wong B, Horn EJ, Krueger GG. Psoriatic arthritis is a strong predictor of sleep interference in patients with psoriasis. Journal of the American Academy of Dermatology. 2009;60(4):604-8.
8. Soldatos CR, Dikeos DG, Paparrigopoulos TJ. Athens Insomnia Scale: validation of an instrument based on ICD-10 criteria. Journal of psychosomatic research. 2000;48(6):555-60.
9. Betteridge N, Boehncke WH, Bundy C, Gossec L, Gratacós J, Augustin M. Promoting patient-centred care in psoriatic arthritis: a multidisciplinary E uropean perspective on improving the patient experience. Journal of the European Academy of Dermatology and Venereology. 2016;30(4):576-85.
10. Gezer O, Batmaz İ, Sariyildiz MA, Sula B, Ucmak D, Bozkurt M, et al. Sleep quality in patients with psoriatic arthritis. International journal of rheumatic diseases. 2017;20(9):1212-8.
11. Hojgaard P, Christensen R, Dreyer L, Mease P, de Wit M, Skov L, et al. Pain mechanisms and ultrasonic inflammatory activity as prognostic factors in patients with psoriatic arthritis: protocol for a prospective, exploratory cohort study. BMJ Open. 2016;6(4):e010650.
12. Buysse DJ, Reynolds III CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry research. 1989;28(2):193-213.