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Published in:
Rheumatology

DOI (link to publication from Publisher):
10.1093/rheumatology/keaa780

Publication date:
2021

Document Version
Accepted author manuscript, peer reviewed version

COMORBIDITIES, PAIN AND FATIGUE IN PSORIATIC ARTHRITIS, PSORIASIS AND HEALTHY CONTROLS: A CLINICAL COHORT STUDY

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Registration numbers:

The Danish National Committee on Health Research Ethics: H-15009080.

Data Protection Agency: 2012-58-0004.

ClinicalTrials.gov: NCT02572700.

Key words: Psoriatic arthritis, comorbidities, tumour necrosis factor inhibitor, pain, fatigue

Key messages:

- Obesity, hypertension and Charlson Comorbidity Index were prognostic factors for poorer treatment outcomes.
- Pain and fatigue were more frequently reported in PsA compared with psoriasis and healthy controls.
- Appropriate screening and management of comorbidities may improve clinical outcomes.

Objectives

To explore the prognostic value of pre-specified comorbidities on treatment outcomes in psoriatic arthritis (PsA), and to compare baseline data with cutaneous psoriasis without arthritis and healthy controls (HC).

Methods

Patients initiating conventional synthetic/biological disease-modifying antirheumatic drugs were enrolled in this clinical observational cohort study, and data on comorbidities, and clinical and patient-reported outcomes were retrieved at baseline and after 4 months. Pearson's chi-squared tests were performed to investigate the prognostic value of pre-specified comorbidities and achievement of ACR20, DAPSA50 and MDA. Mann-Whitney U tests were used to compare Outcome Measures in Rheumatology (OMERACT) PsA Core Outcome Set (COS) measures at baseline and follow-up for the pre-specified comorbidities.

Results

A total of 100 PsA patients were included at baseline. Statistically significantly fewer patients with obesity achieved DAPSA50 compared with patients without obesity (p=0.035), and fewer patients with hypertension (p=0.034) and Charlson Comorbidity Index (CCI) ≥1 (p=0.027), respectively, achieved MDA compared with patients without these comorbidities. Patients with obesity, hypertension, widespread pain, and CCI ≥1 had significantly worse COS measures at follow-up compared with patients without these comorbidities. At baseline, patients with PsA had higher disease burden compared with patients with cutaneous psoriasis and HC, including higher pain (p <0.001) and fatigue (p <0.001) scores, and more widespread pain (p=0.002).

Conclusion

Obesity, hypertension and CCI ≥1 were prognostic factors for poorer treatment outcome rates in PsA. Pain and fatigue were more frequently reported among patients with PsA compared with patients with cutaneous psoriasis and HC.

INTRODUCTION

Psoriatic arthritis (PsA) is a chronic immune-mediated inflammatory disease with a heterogeneous clinical presentation involving joints, entheses, nails and skin (1). Increasing evidence supports the association between PsA and several comorbidities, including cardiovascular disease (CVD), obesity, hypertension and diabetes (2). Additionally, a higher frequency of depression and anxiety is seen in PsA compared with individuals without PsA (3).

Comorbidities such as hypertension, obesity, and depression/anxiety have previously been identified as negative prognostic factors for clinically relevant treatment outcomes in PsA (4–12), and comorbidities significantly impact patients' quality of life (13). Moreover, the presence of comorbidities according to the Charlson Comorbidity Index (CCI) and other comorbidity scores have been associated with higher disease activity, shorter treatment persistence and/or reduced clinical treatment response rates (14–18). Thus, growing evidence indicates that comorbidities play an important role in PsA concerning disease activity and response to treatment.

In 2016 the Outcome Measures in Rheumatology (OMERACT) group updated the PsA Core Outcome Set (COS). Patients and physicians included both inflammatory disease activity and aspects of life impact when identifying the domains of importance in PsA, e.g. pain, fatigue and physical function were rated as key domains by patients. OMERACT recommend that these core domains are included as outcomes in all randomised controlled trials and longitudinal observational studies of PsA (19).

The objective of this observational cohort study was to explore whether pre-specified comorbidities at baseline were prognostic factors for treatment outcomes, including the OMERACT PsA COS. We also aimed to assess the presence of comorbidities, work status, lifestyle factors, and pain and fatigue status of the PsA cohort and compare these baseline characteristics with two control populations: I) a population with cutaneous psoriasis without arthritis, and II) a population of healthy controls (HC).

METHODS

Analysis plan and study design

Methods of the analysis were specified in advance and documented in a study protocol, which was made publicly available at the website of our research institution (www.parkerinst.dk). Findings were reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement (20). Data was obtained from an ongoing PsA cohort, which is

registered at ClinicalTrials.gov (NCT02572700) and approved by the Danish ethics committee (H-15009080) and the Data Protection Agency (2012-58-0004). The study complies with the Declaration of Helsinki.

Participants

We recruited patients with PsA scheduled to start conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) or biologic DMARDs (bDMARDs) from rheumatology clinics in the Capital Region of Denmark and Region Zealand. Patients were ≥18 years old, signed an informed consent form, fulfilled the Classification Criteria for PsA (CASPAR) (21) and presented with peripheral PsA manifestations. Exclusion criteria were pregnancy, peripheral neuropathy, demyelinating disease, stroke within 3 months from baseline, and inflammatory rheumatic diseases besides PsA. Patients were non-eligible if they could not pause glucocorticoids, centrally acting analgesics, and non-opioid analgesics at 21, 7 and 1 days before baseline, respectively. Baseline visits for PsA patients were defined as the time window from 14 days before until 7 days after treatment start. No washout period was required for patients switching therapy. Follow-up for patients with PsA was 4 months after baseline.

Control populations

We included I) 20 patients with cutaneous psoriasis without arthritis from the Department of Dermatology, Bispebjerg Hospital, Copenhagen University Hospital, and II) 20 HCs via public advertisements. Exclusion criteria for the control populations were pregnancy, peripheral neuropathy, demyelinating disease, stroke within 3 months from baseline, inflammatory rheumatic diseases, and current treatment with bDMARDs. Control persons were also non-eligible if they could not pause glucocorticoids, centrally acting analgesics, and non-opioid analgesics at 21, 7 and 1 days before baseline, respectively. All participants were ≥18 years old and signed an informed consent form before inclusion.

Variables

Comorbidities: At baseline, all patients answered questionnaires on a touch screen and provided information on the presence or absence of the following pre-specified current comorbidities: Diabetes, any cancer disease, CVD, hypertension, obesity (calculation based on patient-reported height and weight and defined as ≥30 kg/m^2), osteoporosis, current pharmacological treatment of asthma, and current pharmacological or non-pharmacological treatment of a mental disorder, e.g. depression, anxiety. The selection of comorbidities was based on previous research regarding

comorbidities as prognostic factors for treatment outcomes in PsA (5,7,8,10–12,14,18) and on expected frequencies of the various comorbidities (2). It was prioritized that the comorbidities were relatively frequent among patients with PsA.

Interview and clinical examination: A physician collected information on current and previous medication for rheumatic disease and assessed the CCI score, which was based on the patients' medical history during their lifetime. The physician performed 66/68 swollen/tender joint count (SJC/TJC), Spondyloarthritis Research Consortium of Canada enthesitis index (SPARCC) enthesitis score (22), a manual tender point count (TPC) examination (23), and Psoriasis Area Severity Index (PASI) score (24).

Lifestyle factors: Patients provided on touch screen information on the current use of mild analgesics (paracetamol and acetylsalicylic acid), NSAIDs and opioids, smoking status, alcohol habits, physical activity, education, and work status.

Questionnaires: Health Assessment Questionnaire Disability Index (HAQ-DI) (25), Generalized Anxiety Disorder questionnaire (GAD-10) (26), PainDETECT questionnaire (27), the Medical Outcomes Study Short Form (SF)-36 questionnaire (28), Psoriatic Arthritis Impact of Disease (PsAID) (29) (PsA patients only), Dermatology Life Quality Index (DLQI) (30) (PsA and psoriasis patients only), visual analogue scales (VAS) of pain, fatigue, and patient global.

Assessment of widespread pain: According to the 2016 fibromyalgia criteria (31), we defined widespread pain (WP) as a WP Index (WPI) score ≥4 and with a pain distribution of ≥4/5 regions at the WPI or the painDETECT (27) drawing. If there was inconsistency between the WPI drawing and the painDETECT drawing, making it difficult to determine if the patient satisfied the WP criteria, we evaluated if other signs of pain hypersensitivity were present, i.e. any of the following features: I) painDETECT score ≥13 (27); II) SJC/TJC ratio <0.5 (32); or III) TPC ≥8 (33). In total, 21 patients were difficult to classify, and drawings of these patients were evaluated by consensus of co-authors (KA, LEK, CB).

Paraclinical measures: A blood test was drawn to measure haemoglobin, cholesterol (total), glycated haemoglobin (HbA1c), alanine aminotransferase (ALAT), and C-reactive protein (CRP).

Prognostic factors of interest and outcome measures

Prognostic factors: The following covariates, defined as described in the section above, were included in the current study: Asthma, any cancer disease, CVD, diabetes, hypertension, obesity, osteoporosis, mental disorder, WP, and CCI ≥1.

Outcome measures: At follow-up, i.e. 4 months after baseline, the primary treatment outcome, American College of Rheumatology 20% improvement criteria (ACR20) (34) and the secondary treatment outcomes, 50% improvement in Disease Activity index for PSoriatic Arthritis (DAPSA50) (35) and Minimal Disease Activity (MDA) (36) were assessed. Furthermore, the OMERACT PsA COS (19) at baseline and follow-up was assessed (10).

Statistical analyses

Demographic and descriptive data were presented as mean and standard deviation, median and interquartile ranges, or numbers and percentages. Groups were compared by parametric tests (Student's t-test, one-way independent ANOVA) if data followed a normal distribution, otherwise non-parametric tests (Pearson's chi-squared test, Fisher's exact test, Mann Whitney U test, Kruskal-Wallis test). In all statistical tests, p values <0.05 (two sided) were considered statistically significant. If the number of expected values in any of the cells of the contingency table were ≥5, Pearson's chi-squared tests were performed to investigate the association between the pre-specified comorbidities and achievement of ACR20, DAPSA50 and MDA, otherwise we used Fisher's exact test. Analyses were based on the intention-to-treat (ITT) population, e.g. non-responder imputation in case of missing data. As data were non-normally distributed, we performed Mann-Whitney U tests to compare OMERACT PsA COS measures for the pre-specified comorbidities at baseline and follow-up. If the number of comorbidities were <5 in the PsA cohort, we abstained from performing statistical analyses on the impact of the comorbidities on treatment outcomes. In the main article we present results for the pre-specified comorbidities that had a frequency of ≥20 in the PsA cohort. Results for comorbidities with a frequency <20 are interpreted as underpowered and presented in supplementary material.

RESULTS

Patient inclusion. A total of 181 Danish PsA patients were screened for eligibility, and 100 PsA patients were included at baseline. The number of patients who withdrew from the study was 16% (Figure S1 and S2).

Baseline data. Demographics and disease characteristics of the cohort and the control populations are shown in Table 1. PsA patients had the highest disease burden including levels of pain, fatigue, use of analgesics, more WP and higher CRP, SJC, TJC, SPARCC enthesitis scores followed by patients with psoriasis, and HC had the lowest disease burden of the three groups. Patients with PsA initiated a csDMARD in 44% of the cases and 73% were bDMARD-naïve at baseline. We did not observe statistically significant differences between the number of patients that initiated csDMARD and bDMARD among comorbidity subgroups (e.g. obese versus non-obese). Nonetheless, patients with obesity, CCI ≥1 and WP had a statistically significantly more frequent use of mild analgesics, while patients with hypertension and CCI ≥1 had a more frequent use of opioids compared with patients without these comorbidities (Table S6 and S7).

Response data. Table 2 and figure 1 present the number of ACR20, DAPSA50 and MDA responders according to the pre-specified comorbidities with number of events ≥20. Hypertension, obesity and CCI ≥1 were statistically significantly associated with poorer outcome rates. Table S1 and figure S3 present the number of responders according to comorbidities where the number of events were <20. None of the patients that reported current treatment of a mental disorder (n=9) achieved ACR20 (p=0.029).

OMERACT PsA COS measures. Table 3 and 4 present the difference between COS measures at baseline and follow-up for obesity, hypertension, WP and CCI, respectively. Overall, patients with obesity and hypertension, respectively, had a non-significantly higher disease burden at baseline compared with patients without these comorbidities and at follow-up they had statistically significantly higher disease burden compared with patients without these comorbidities. Patients with WP and CCI ≥1, respectively, had significantly higher disease burden compared with patients without these comorbidities at baseline and follow-up.

Table S2, S3 and S4 present the difference between COS measures in patients with asthma, CVD, diabetes, mental disorder, osteoporosis, and CCI ≥2 at baseline and follow-up, respectively. Overall, patients that reported current treatment of a mental disorder had a non-significantly higher disease burden at baseline compared with patients that did not report current treatment of a mental disorder, and at follow-up they had a statistically significantly higher disease burden compared with patients that did not report current treatment of a mental disorder. For CVD, diabetes, asthma, osteoporosis and CCI ≥2, there were very few significant differences between groups.

Additional analyses. In a post hoc analysis, we found that patients that reported current treatment of a mental disorder (n=9) had baseline median GAD-10, SF-36 mental component summary (MCS) and SF-36 mental health (MH) of 18 (interquartile range (IQR) 15-22), 34 (IQR 26-45) and 36 (IQR 28-60), respectively, and these values were statistically significantly different from the values of the patients that did not report current treatment of a mental disorder (table S5).

DISCUSSION

In this observational clinical cohort study of 100 Danish PsA patients initiating cs/bDMARD therapy, we report that obesity, hypertension and CCI ≥1 were prognostic factors for poorer treatment outcome rates in PsA. Baseline values showed that patients with PsA had higher disease burden including higher scores of pain and fatigue compared with patients with cutaneous psoriasis without arthritis and HC. The results suggest that patients with comorbidities were less likely to respond well in the domains that are rated as most important by PsA patients such as pain and fatigue (19,29).

Previous studies report that obesity is associated with poorer tumour necrosis factor (TNF) inhibitor (TNFi)-treatment outcomes (5,7,8,12), whereas a retrospective study including TNFi-treated PsA patients (37), a study of abatacept-treated PsA patients (38), and a recently published study on interleukin (IL)-23 and IL-17 inhibitors (18) did not. Our results lend support to the evidence of an association between obesity and treatment response. Obesity may be linked to PsA through different underlying mechanisms. Obesity is characterized by chronic low-grade inflammation that is driven by the adipose tissue, which is metabolically active and secretes cytokines such as TNF-alpha, which is also involved in PsA (39). Furthermore, a higher occurrence of biomechanical stress on the joints and tendons among obese patients may be of importance (7,40). Moreover, evidence suggests that obesity is positively associated with chronic pain (40), which may result in a lower likelihood of achieving outcomes that include pain and TJC in the score (7). Our results are in line with this assumption, because the non-obese patients improved in pain and TJC scores after 4 months, while the obese patients did not improve in theses scores. Finally, it has been debated whether dose escalation could simply improve the treatment outcomes in patients with obesity, but this theory was not confirmed in a previous mentioned relatively large register study (8). There is currently evidence for a higher rate of MDA achievement and reduced disease activity after weight loss in PsA (41,42). Consequently, management of obesity seems important for optimal care of patients with PsA.

We also found a statistically significant association between hypertension and decreased ability to achieve MDA, and the OMERACT PsA COS measures for patients with hypertension were worse after 4 months' of treatment compared with patients without hypertension. These results are in line with a previous cohort study reporting that patients with hypertension were less likely to achieve remission defined as Clinical Disease Activity Index (CDAI) ≤2.8 (12). Moreover, we found a signal towards lower ability to achieve MDA among patients with WP and a statistically significant difference in COS measures at baseline and follow-up between patients with and without WP, an association which was previously thoroughly explored (10).
Also, a statistically significant association between CCI ≥1 and the ability to achieve MDA was demonstrated, and the COS measures for patients with CCI ≥1 were worse after 4 months' of treatment compared with patients with CCI=0. Other studies have investigated the association between presence of comorbidities and treatment outcomes in PsA. One previous study found no association between the presence of any of 17 pre-specified comorbidities at baseline and European League Against Rheumatism (EULAR) response (43). By contrast, other studies did report association between comorbidities (assessed by use of CCI, modified Rheumatic Disease Comorbidity Index (mRDCI) or number of comorbidities) and disease activity and/or composite outcomes including EULAR response and MDA (14,15,17,18). Our results support the importance of monitoring and treating comorbidities in PsA, as suggested in the treatment recommendations from EULAR and the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) (44,45).

None of the patients that reported current treatment of a mental disorder achieved ACR20 or MDA, and these patients had statistically significantly worse COS outcomes after 4 months' of treatment compared with patients that did not report current treatment of a mental disorder. It is important to notice that only 9% of the PsA patients reported current treatment of mental disorder. However, although based on a small sample, the findings indicate an association between mental disorders and poorer treatment outcomes and are in line with a previous cohort study (11). That study included 1326 patients with RA and 728 patients with PsA and investigated the predictive value of baseline depression/anxiety on the likelihood of achieving remission. All results were significant for RA ($p \leq 0.008$), while some results were significant for PsA (p from 0.001 to 0.73), depending on the various remission and depression/anxiety criteria applied (11). In another previous register study of 1750 patients with PsA, our research group demonstrated poorer treatment persistence for patients with a diagnosis at baseline of depression and/or anxiety (14). Additionally, there is increasing evidence that depression and anxiety are linked with higher levels of serum IL-17 and TNF-alpha (46), which are cytokines that are also involved in PsA (1). The signals towards a possible impact of

psychological distress on treatment outcomes needs further attention and is of particular importance, because mental disorders frequently occurs in PsA patients and may be treatable (3). Improved identification and management of mental disorders may lead to better clinical outcomes.

In the current study, we reported data on the COS measures at baseline and follow-up. However, it is important to notice that in many cases the patients with obesity, hypertension, WP, CCI ≥1 and mental disorder did improve in COS outcomes after 4 months of treatment, but the baseline values were often higher for patients with comorbidities compared with patients without comorbidities. Thus, for some domains, the patients with comorbidities had poorer COS outcomes at follow-up, because they had a higher disease burden at baseline compared with patients without these comorbidities. It is also important to notice that a considerably proportion of the patients with comorbidities achieved the treatment outcomes. Furthermore, we observed that patients with obesity, hypertension or a CCI ≥1 had statistically significantly lower response rates for some treatment outcomes, but not for other. While the reason for this finding remains enigmatic, one possible explanation could rely on the different composition of the treatment outcomes. Although the outcomes include many of the same domains there are differences between them, and additionally, ACR20 and DAPSA50 are measures of change, whereas MDA is a disease state. However, for all the pre-specified comorbidities where the number of events were ≥20, we observed (significantly or non-significantly) lower response rates for patients with comorbidities compared with patients without comorbidities, regardless of the chosen treatment outcome.

We also investigated if other pre-specified comorbidities such as asthma, CVD, diabetes, osteoporosis, and a CCI ≥2 influenced treatment outcomes. Since the main results showed an association between CCI ≥1 and MDA, we did also expect to observe an association between CCI ≥2 and MDA. However, we did not find an association between any of the abovementioned comorbidities and treatment outcomes, nor any noteworthy differences in OMERACT PsA COS measures between groups. These findings may reflect that no true association between these comorbidities and treatment outcomes existed or they may be a result of limited statistical power due to a low number of events.

In this study, baseline data for the PsA cohort was compared with two control populations. Patients with PsA presented with a statistically significantly higher symptom burden; higher levels of pain, fatigue, disability, use of analgesics, more WP, and higher CRP, SJC, TJC, and SPARCC enthesitis score compared with patients with cutaneous psoriasis without arthritis, and patients with cutaneous

psoriasis had higher scores of these variables compared with HC. Even though the patients with cutaneous psoriasis had the highest BMI and the highest levels of most comorbidities, patients with PsA still had the highest symptom burden. However, a higher BMI and comorbidity level may potentially explain why patients with cutaneous psoriasis had higher levels of some of the variables, e.g. pain (40), compared with HC. Patients with PsA had higher levels of sick leave compared with the HC, which is in line with previous research (47). Furthermore, patients with PsA had a notably higher frequency of comorbidities compared with the HC and a proportion of the increased disease burden experienced by the PsA patients may be attributed comorbidities rather than PsA, i.e. we did not adjust for the influence of comorbidities on the variables. Some of the most important domains for patients with PsA are pain and fatigue (19,29), and it was also within these domains that patients with PsA differed from patients with cutaneous psoriasis and HC.

An important limitation was limited statistical power due to relatively few participants. Moreover, when compared with a previously published study of comorbidities in PsA (2), we found a low prevalence of comorbidities among the PsA patients in our cohort. When compared with a report of the general population in Denmark, the PsA patients had higher occurrence of all comorbidities except cancer, while our HC had lower occurrence of nearly all comorbidities (48). This may be because our patients and HC mostly were recruited from the Frederiksberg area, where the population in general has a better somatic health status compared with other parts of the country (48). The current study was based on prospectively collected observational real-life data from patients recruited from specialized departments of rheumatology and dermatology, and the results may not be generalisable to the overall referral population. Another important limitation of the study was that data on comorbidities was reported by the patients. Also, the 4-month response rates, especially MDA, were relatively low (~20%) compared with other observational studies (49), however, in line with a recently published clinical outpatient cohort study from Norway in which MDA was achieved by 22.9% of the patients (50). Although we did not observe statistically significant differences between the number of patients that initiated csDMARD and bDMARD among comorbidity subgroups (e.g. obese versus non-obese), the patients with obesity, hypertension, CCI ≥1 and WP had a more frequently use of analgesics compared with patients without these comorbidities. Finally, we did not correct for multiple testing. The abovementioned limitations may have influenced our understanding of the associations between comorbidities and treatment outcomes, and the results of the current study must be interpreted with care.

The strengths of the current study include the application of PsA specific response measures such as MDA and the OMERACT PsA COS. Nonetheless, a recommended set of instruments that adequately assess the PsA COS is currently under development and measures of the COS were therefore chosen based on their common use, availability in the current study and a previously published paper from our research group (10). At baseline, we also presented the occurrence of comorbidities, lifestyle factors, work status, and disease-related and patient-reported outcomes of patients with cutaneous psoriasis without arthritis and HC, which provided important insight into PsA patients' baseline values relative to the control populations.

In this observational clinical cohort study of 100 Danish patients with PsA initiating cs/bDMARD therapy, we report that obesity, hypertension and CCI ≥1 were prognostic factors for poorer treatment outcome rates in PsA. At baseline, patients with PsA had higher disease burden including higher scores of pain and fatigue compared with patients with cutaneous psoriasis without arthritis and HC. The results are in line with previous studies in the field and emphasize the importance of managing and treating comorbidities in patients with PsA in order to treat the patient to target.

DATA AVAILABILITY

The data underlying this article cannot be shared publicly due to the privacy of the individuals that participated in the study. All authors have access to the data.

CONFLICTS OF INTEREST

CB has no conflicting interests.
MS has no conflicting interests.
JGM has received fees for speaking from AbbVie, Novartis, Eli Lilly and BK Ultrasound.
CVN has received educational grants from AbbVie.
KA has no conflicting interests.
TSJ has received fees for speaking from Abbvie, Pfizer, Roche, Biogen, Novartis, UCB and Eli Lilly.
LD has received grant/research support from: Unrestricted grant from BMS, Consultant of: Janssen Pharmaceutica, Speaking fees/consultancy: UCB, MSD and Eli-Lilly.
LEK has received fees for speaking and consultancy from Pfizer, AbbVie, Amgen, UCB, Celegene, BMS, MSD, Novartis, Eli Lilly, and Janssen pharmaceuticals.

CONTRIBUTIONS OF AUTHORS

Contributions: All authors contributed to the study conception and design, the analysis and interpretation of data, the revision of the manuscript and the approval of the final version. All authors had access to data in the study period. CB drafted the manuscript, and CB and LEK take the overall responsibility for the scientific integrity of the work.

FUNDING

This work was supported by unrestricted grants from the Oak foundation; the Danish Psoriasis Association; Muskellaboratoriets Fond; Clara Hansens Mindelegat; and Bispebjerg and Frederiksberg Hospital.

ACKNOWLEDGEMENT

We wish to thank all persons who participated in the current study. Furthermore, we thank Christian Cato and Peter Krusager for data management support, Eva Wæhrens for data interpretation support, and finally we thank all previous and current clinical staff from the Parker Institute. We also thank the clinical departments for assisting with recruitment of participants.

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Table 1. Patient characteristics at baseline.

	PsA (n = 100)	Psoriasis (n = 20)	Healthy controls (n = 20)	p
Demographics characteristics and lifestyle				
Women, n (%)	59 (59)	10 (50)	10 (50)	0.63
Age (years), mean (SD)	52.0 (13.5)	52.3 (15.4)	52.2 (13.0)	0.99
Body mass Index (BMI) (kg/m^2), mean (SD)	26.6 (5.4)	29.6 (5.2)	23.8 (3.2)	0.002
Longer education after high school, n (%)	35 (36)	7 (35)	10 (50)	0.47
Work status, n (%)				
Working full-time, n (%)	41 (42)	5 (25)	14 (70)	0.013
Sick leave, n (%)	11 (11)	0 (0)	0 (0)	0.14
Daily alcohol use, n (%)	2 (2)	0 (0)	1 (5)	0.64
Smoking, n (%)	25 (25)	7 (35)	5 (25)	0.64
Physical activity min. 4 days per week, n (%)	51 (52)	10 (50)	18 (90)	0.006
Current comorbidities				
Asthma, n (%)	10 (10)	4 (20)	0 (0)	0.10
Diabetes, n (%)	6 (6)	1 (5)	0 (0)	0.83
Any cancer, n (%)	1 (1)	2 (10)	0 (0)	0.11
Cardiovascular disease, n (%)	6 (6)	3 (15)	0 (0)	0.16
Hypertension, n (%)	29 (29)	5 (25)	4 (20)	0.67
Obesity, n (%)	22 (22)	10 (50)	1 (5)	0.004
Osteoporosis, n (%)	6 (6)	1 (5)	1 (5)	0.99
Mental disorder, n (%)	9 (9)	2 (10)	0 (0)	0.49
Charlson comorbidity index (CCI)				
CCI = 0	65 (65)	12 (60)	17 (85)	0.17
CCI = 1	22 (22)	4 (20)	2 (10)	0.59
CCI ≥ 2	13 (13)	4 (20)	1 (5)	0.37
Patient reported outcomes				
VAS pain (0 – 100 mm)	59 (28-72)	2 (0-6)	0 (0-1)	<0.001
VAS fatigue (0 – 100 mm)	60 (40-80)	19 (4-58)	7 (0-12)	<0.001
VAS patient global (0 – 100 mm)	64 (38-80)	N/A	N/A	N/A
VAS physician global (0 – 100 mm)	55 (40-65)	N/A	N/A	N/A
PsAID-9 (0 - 10)	5.2 (3.0-6.5)	N/A	N/A	N/A
HAQ-DI (0 - 3)	0.88 (0.38-1.25)	0 (0-0.32)	0 (0-0)	<0.001
GAD-10 (0 - 50)	7.0 (5.0-12.0)	5.5 (3.0-11.0)	2.0 (0.0-4.0)	<0.001
DLQI (0 - 30)	1.0 (0.0-4.5)	5.0 (2.0-7.5)	N/A	0.002
Disease related characteristics				
Tender joint count (68)	14 (7-27)	2 (0-2)	0 (0-0)	<0.001
Swollen joint count (66)	5 (3-9)	0 (0-0)	0 (0-0)	<0.001
SPARCC (0 - 16)	4 (2-7)	0 (0-2)	0 (0-0)	<0.001
PASI (0 - 72)*	1.2 (0.3-4.4)	5.0 (2.7-9.0)	N/A	0.002
DAS28-CRP (0-10)	4.25 (3.39-4.91)	N/A	N/A	N/A
Tender point count (0 - 18)	2 (0-5)	0 (0-0)	0 (0-0)	<0.001
Widespread pain, n (%)	23 (23)	0 (0)	0 (0)	0.002
Blood samples				
C-reactive protein (CRP) (mg/L)	4 (1-10)	2.5 (0.8-4.0)	0 (0-1.0)	<0.001
Haemoglobin (mmol/L)	8.7 (8.1-9.3)	8.9 (8.6-9.4)	8.8 (8.7-9.5)	0.14
Cholesterol, total (mmol/L)	4.9 (4.3-5.8)	5.2 (4.5-5.8)	5.4 (4.8-6.0)	0.42
HbA1c (mmol/mol)	36.0 (33.0-38.0)	35.5 (33.5-37.5)	34.5 (32.5-36.0)	0.61
Alanine aminotransferase (ALAT) (U/L)	26.0 (19.0-39.0)	29.0 (21.5-37.5)	26.0 (21.5-30.5)	0.71
Alkaline phosphatase (U/L)	70.0 (58.0-84.0)	71.0 (58.5-91.0)	60.0 (52.5-68.5)	0.060
Treatment				
csDMARD initiator, n (%)	44 (44)	N/A	N/A	N/A
bDMARD naïve, n (%)	73 (73)	N/A	N/A	N/A
Analgesics 4-7 days per week, n (%)				
Mild analgesics	35 (35)	2 (10)	1 (5)	0.004
NSAIDs	31 (31)	1 (5)	1 (5)	0.003
Opioids	7 (7)	0 (0)	0 (0)	0.57

Table 2. Number of patients achieving ACR20, DAPSA50 and MDA according to comorbidity.

		ACR20		DAPSA50		MDA	
	n*	**Responders (n, %)**	**p**	**Responders (n, %)**	**p**	**Responders (n, %)**	**p**
Hypertension	29	9 (31)	0.99	8 (28)	0.20	1 (3)	**0.034**
No hypertension	70	23 (33)		29 (41)		15 (21)	
Obesity	22	6 (27)	0.57	4 (18)	**0.035**	2 (9)	0.51
No obesity	77	26 (34)		33 (43)		14 (18)	
Widespread pain	23	7 (30)	0.77	7 (30)	0.39	1 (4)	0.11
No widespread pain	77	25 (34)		31 (40)		16 (21)	
CCI ≥1	35	10 (29)	0.49	12 (34)	0.57	2 (6)	**0.027**
CCI = 0	65	23 (35)		26 (40)		15 (23)	

Responses are intention-to-treat (ITT). p values <0.05 are marked with bold. ACR20, American College of Rheumatology 20% improvement criteria; DAPSA50, 50% improvement in Disease Activity index for PSoriatic Arthritis; MDA, Minimal Disease Activity; CCI, Charlson Comorbidity Index. *One patient did not provide information on presence or absence of current comorbidities at baseline, but the patient did participate in the laboratory and clinical assessments including assessment of widespread pain and CCI score.

Table 3. COS measurements at baseline and 4-months follow-up according to obesity and hypertension.

	Baseline			Follow-up		
	Obese (n = 22)	**Non-obese (n = 77)**	**p**	**Obese (n = 22)**	**Non-obese (n = 77)**	**p**
MSK disease activity						
SJC (66)	6 (3-11)	5 (3-8)	0.48	4 (1-8)	2 (1-5)	0.38
TJC (68)	11 (7-27)	15 (7-27)	0.92	12 (6-19)	7 (2-15)	**0.037**
SPARCC enthesitis	4 (2-6)	4 (2-7)	0.94	5 (1-9)	4 (1 -6)	0.20
Skin disease						
PASI	1.0 (0.4-2.3)	1.3 (0.3-5.4)	0.39	0.6 (0.0-1.4)	0.6 (0.0-1.6)	0.92
Pain						
VAS pain	70 (50-78)	50 (27-71)	**0.016**	60 (21-77)	26 (10-61)	**0.008**
SF36 Bodily Pain	41 (22-52)	41 (22-61)	0.64	41 (31-52)	52 (41-82)	**0.025**
Physical function						
SF-36 PF	55 (40-60)	60 (45-80)	0.20	57.5 (30-65)	75 (55-85)	**0.009**
HAQ-DI	1.0 (0.75-1.25)	0.88 (0.38-1.25)	0.46	1.00 (0.38-1.25)	0.50 (0.13-1.00)	**0.031**
Health-related QoL						
DLQI	1 (1-4)	1 (0-5)	0.94	1 (0-1)	1 (0-3)	0.45
PsAID-9	6.0 (4.0-6.5)	5.0 (2.9-6.4)	0.13	4.8 (3.8-6.5)	2.9 (1.3-5.0)	**0.005**
Patient Global						
Patient Global VAS	68 (53-80)	62 (37-78)	0.28	65 (50-80)	33 (9-61)	**0.003**
Fatigue						
NRS Fatigue	8 (5-8)	6 (3-8)	**0.031**	6 (4-8)	5 (1-7)	**0.031**
SF-36 Vitality Scale	33 (25-50)	35 (25-60)	0.31	38 (25-55)	50 (30-75)	0.055
Systemic inflammation						
CRP (mg/L)	5 (2-12)	4 (1-9)	0.38	4 (2-7)	2 (1-5)	**0.016**
	Hypertension (n = 29)	**No hypertension (n = 70)**	**p**	**Hypertension (n = 29)**	**No hypertension (n = 70)**	**p**
MSK disease activity						
SJC (66)	8 (3-10)	5 (3-7)	0.094	3 (1-6)	2 (1-5)	0.39
TJC (68)	16 (11-27)	13 (6-27)	0.14	10 (6-25)	7 (2-16)	**0.044**
SPARCC enthesitis	5 (3-7)	4 (2-6)	0.16	5 (1-9)	4 (1-6)	0.082
Skin disease						
PASI	1.0 (0.3-5.4)	1.3 (0.3-4.0)	0.96	1.0 (0.0-1.6)	0.4 (0.0-1.5)	0.29
Pain						
VAS pain	64 (35-72)	50 (26-72)	0.14	56 (21-71)	25 (7-63)	**0.026**
SF-36 Bodily Pain	41 (31-52)	41 (22-61)	0.83	42 (31-62)	52 (41-82)	0.20
Physical function						
SF-36 PF	55 (40-65)	60 (45-80)	0.093	55 (45-75)	75 (55-85)	**0.023**
HAQ-DI	0.88 (0.38-1.25)	0.88 (0.38-1.25)	0.75	0.88 (0.38-1.13)	0.50 (0.13-1.00)	0.058
Health-related QoL						
DLQI	1 (0-4)	1 (0-6)	0.47	1 (0-2)	1 (0-3)	0.98
PsAID-9	5.8 (4.3-6.5)	5.0 (2.9-6.5)	0.20	4.6 (2.5-6.2)	3.2 (1.1-5.4)	**0.041**
Patient Global						
Patient Global VAS	70 (54-79)	62.5 (32-80)	0.20	54 (41-69)	32 (8-68)	0.051
Fatigue						
NRS Fatigue	8 (6-8)	6 (3-8)	**0.013**	6 (4-8)	4.5 (1-7)	**0.040**
SF-36 Vitality Scale	35 (25-50)	35 (25-65)	0.57	40 (25-55)	50 (30-75)	0.16
Systemic inflammation						
CRP (mg/L)	6 (2-10)	3 (1-9)	0.26	3 (2-4)	2 (1-6)	0.30

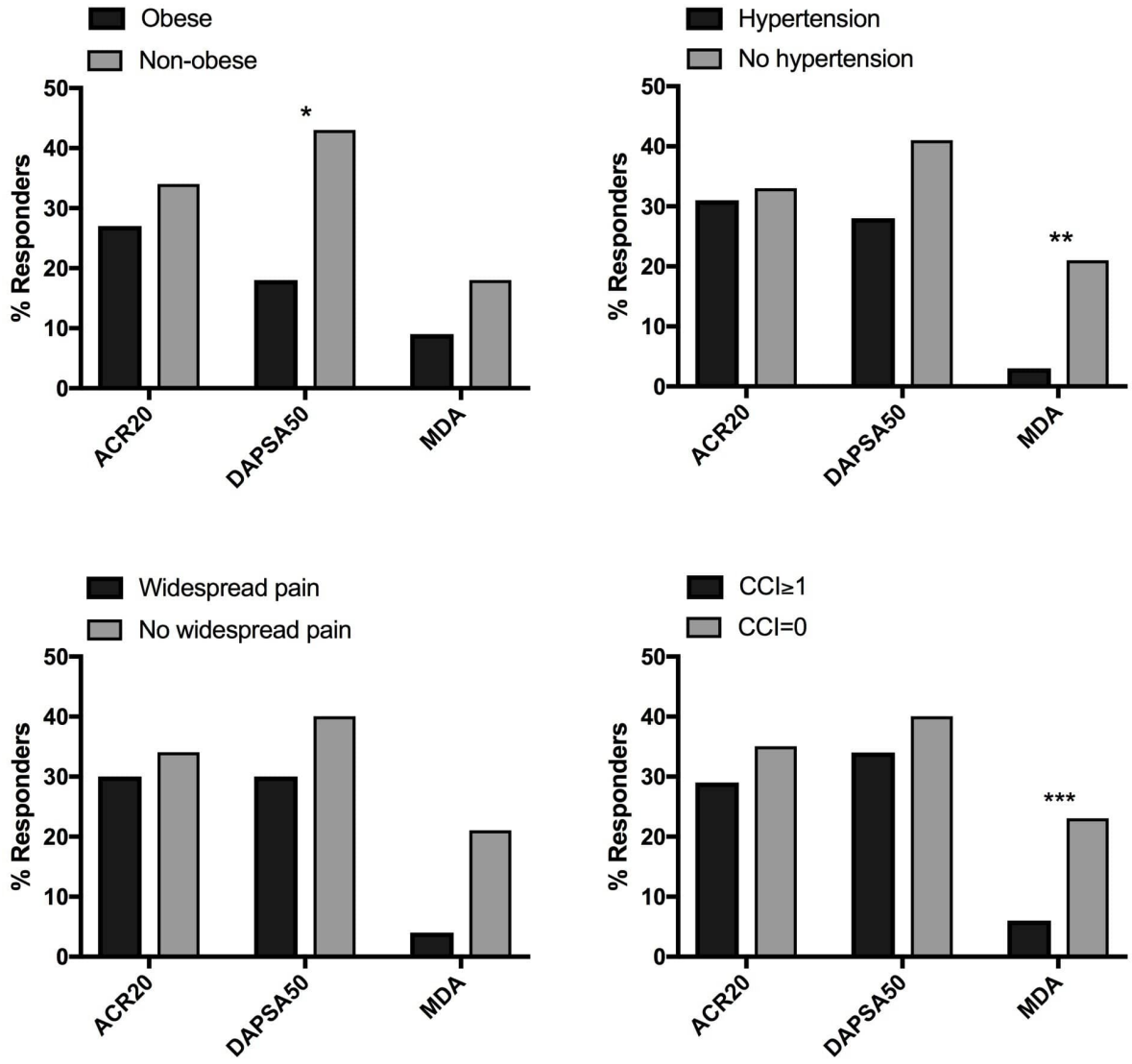
Values are intention-to-treat (ITT) and presented as median (interquartile range). p values <0.05 are marked with bold. COS, core outcome set; MSK, musculoskeletal disease; SJC, swollen joint count; TJC, tender joint count; SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index; PASI, Psoriasis Area Severity Index; VAS, visual analogue scale; PF, physical function; SF-36, Short-form 36 questionnaire; HAQ-DI, Health Assessment Questionnaire Disability Index; QoL, quality of life; DLQI, Dermatology Life Quality Index; PsAID, Psoriatic Arthritis Impact of Disease; NRS, numerical rating scale; CRP, C-reactive protein.

Table 4. COS measurements at baseline and 4-months follow-up according to widespread pain and CCI.

	Baseline			Follow-up		
	WP (n = 23)	**No WP (n = 77)**	**p**	**WP (n = 23)**	**No WP (n = 77)**	**p**
MSK disease activity						
SJC (66)	5 (3-10)	6 (2.5-8.5)	0.94	3 (1-5)	2 (1-6)	0.39
TJC (68)	24 (16-29)	12 (7-25)	**0.016**	12 (7-29)	7 (2-13)	**0.005**
SPARCC enthesitis	5 (3-10)	4 (2-6)	**0.046**	5 (4-8)	3 (0-6)	**0.008**
Skin disease						
PASI	0.8 (0.4-3.1)	1.4 (0.3-5.2)	0.39	0.4 (0.0-1.6)	0.6 (0.0-1.5)	0.83
Pain						
VAS pain	70 (59-81)	50 (27-71)	**0.015**	59 (33-70)	24 (7-67)	**0.012**
SF36 Bodily Pain	31 (12-41)	41 (31-62)	**<0.001**	41 (22-52)	61 (41-84)	**0.009**
Physical function						
SF-36 PF	50 (30-55)	60 (45-80)	**<0.001**	50 (35-75)	75 (55-85)	**<0.001**
HAQ-DI	1.25 (0.75-1.88)	0.88 (0.38-1.13)	**0.005**	1.00 (0.38-1.63)	0.50 (0.13-1.00)	**0.004**
Health related QoL						
DLQI	1 (0-5)	1 (0-4)	0.82	1 (1-5)	1 (0-2)	0.063
PsAID-9	6.2 (5.0-7.5)	4.4 (2.9-6.3)	**0.003**	4.7 (3.8-6.0)	2.9 (1.1-5.1)	**0.003**
Patient Global						
Patient Global VAS	76 (60-86)	62 (32-76)	**0.012**	61 (47-78)	32 (8-66)	**0.007**
Fatigue						
NRS Fatigue	7 (6-8)	6 (3-8)	**0.045**	6 (4-8)	4 (2-8)	0.056
SF-36 Vitality Scale	30 (10-40)	40 (25-60)	**0.018**	35 (20-60)	50 (35-75)	**0.011**
Systemic inflammation						
CRP (mg/L)	5 (2-9)	4 (1-11)	0.73	3 (2-6)	2 (1-5)	0.16
	CCI ≥1 (n = 35)	**CCI = 0 (n = 65)**	**p**	**CCI ≥1 (n = 35)**	**CCI = 0 (n = 65)**	**p**
MSK disease activity						
SJC (66)	7 (3-11)	5 (2-8)	**0.036**	3 (1-7)	2 (0-5)	**0.047**
TJC (68)	19 (11-28)	11 (5-26)	**0.026**	10 (6-19)	6.5 (2-16)	0.079
SPARCC enthesitis	5 (2-7)	4 (2-7)	0.70	4 (1-7)	4 (1-6)	0.21
Skin disease						
PASI	1.7 (0.4-6.2)	1.2 (0.1-3.8)	0.40	1.0 (0.0-2.0)	0.5 (0.0-1.5)	0.40
Pain						
VAS pain	64 (33-74)	57 (28-72)	0.23	56 (15-72)	22 (10-61)	**0.028**
SF36 Bodily Pain	31 (22-51)	41 (31-62)	**0.017**	41 (31-62)	62 (42-84)	**0.004**
Physical function						
SF-36 PF	55 (35-65)	60 (45-80)	**0.025**	55 (45-80)	75 (55-90)	**0.011**
HAQ-DI	1.00 (0.63-1.63)	0.88 (0.38-1.25)	**0.064**	1.00 (0.25-1.50)	0.50 (0.13-0.88)	**0.008**
Health related QoL						
DLQI	1 (0-6)	1 (1-4)	0.85	1 (0-5)	1 (0-2)	0.66
PsAID-9	6.0 (4.1-7.3)	4.7 (2.9-6.2)	**0.007**	4.6 (2.5-6.5)	2.9 (1.1-4.8)	**0.004**
Patient Global						
Patient Global VAS	76 (59-89)	57 (32-75)	**0.009**	61 (25-79)	32 (8-60)	**0.008**
Fatigue						
NRS Fatigue	8 (5-8)	6 (3-7)	**0.009**	6 (4-8)	4 (1-7)	**0.008**
SF-36 Vitality Scale	30 (20-50)	40 (25-60)	0.093	35 (25-60)	50 (35-75)	**0.038**
Systemic inflammation						
CRP (mg/L)	4 (1-10)	4 (1-9)	0.80	3 (1-6)	2 (1-5)	0.75

Values are intention-to-treat (ITT) and presented as median (interquartile range). P values <0.05 are marked with bold. COS, core outcome set; CCI, Charlson comorbiditiy index; MSK, musculoskeletal disease; SJC, swollen joint count; TJC, tender joint count; SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index; PASI, Psoriasis Area Severity Index; VAS, visual analogue scale; PF, physical function; SF-36, Short-form 36 questionnaire; HAQ-DI, Health Assessment Questionnaire Disability Index; QoL, quality of life; DLQI, Dermatology Life Quality Index; PsAID, Psoriatic Arthritis Impact of Disease; NRS, numerical rating scale; CRP, C-reactive protein.

Figure 1.


Obese
Non-obese
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MDA
Hypertension
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ACR20
DAPSA50
MDA
Widespread pain
No widespread pain
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ACR20
DAPSA50
MDA
CCI≥1
CCI=0
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MDA

Figure S1:

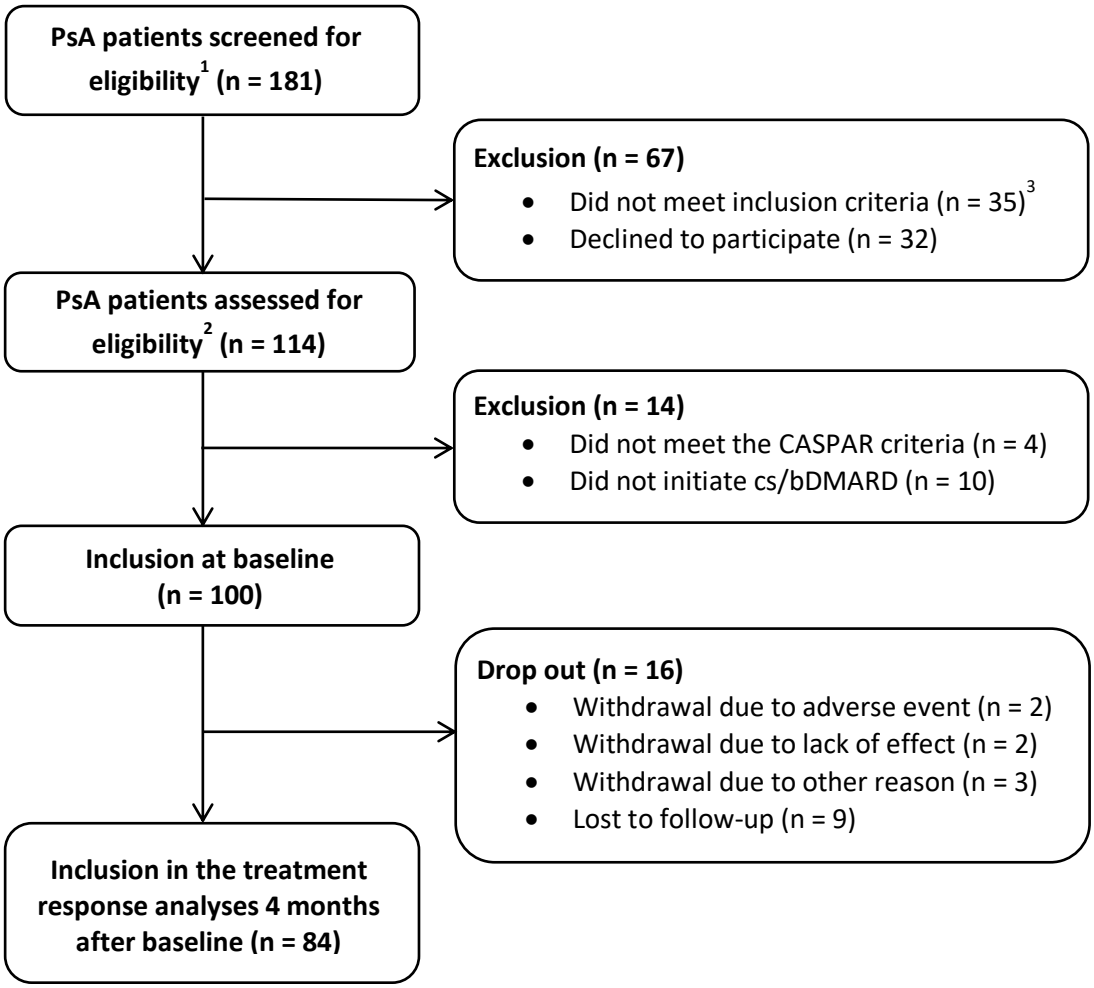

PsA patients screened for eligibility[1] (n = 181)
Exclusion (n = 67)
Did not meet inclusion criteria (n = 35)[3]
Declined to participate (n = 32)
PsA patients assessed for eligibility[2] (n = 114)
Exclusion (n = 14)
Did not meet the CASPAR criteria (n = 4)
Did not initiate cs/bDMARD (n = 10)
Inclusion at baseline (n = 100)
Drop out (n = 16)
Withdrawal due to adverse event (n = 2)
Withdrawal due to lack of effect (n = 2)
Withdrawal due to other reason (n = 3)
Lost to follow-up (n = 9)
Inclusion in the treatment response analyses 4 months after baseline (n = 84)

Figure S2.

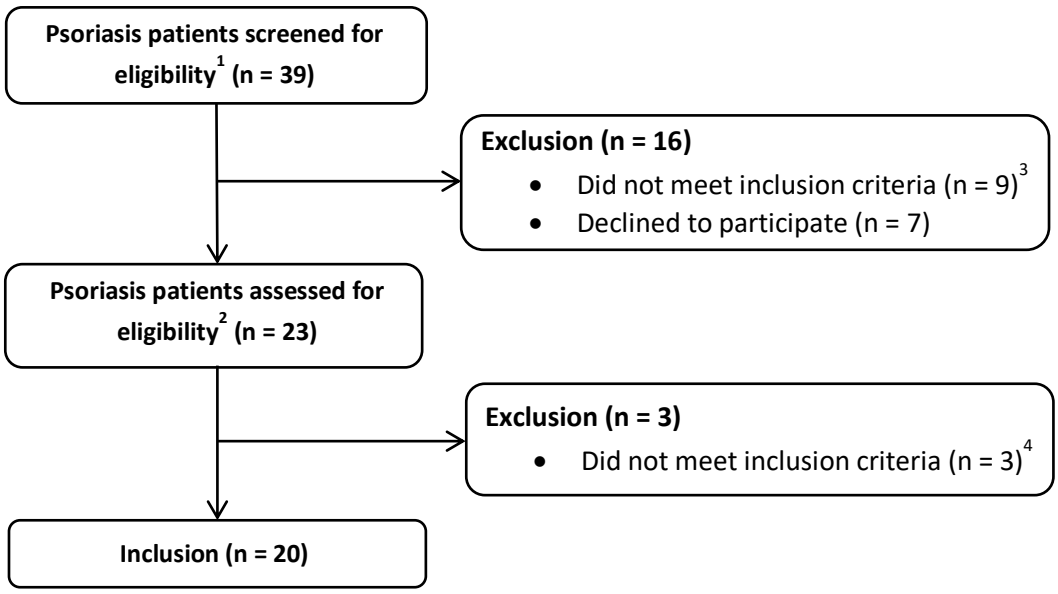
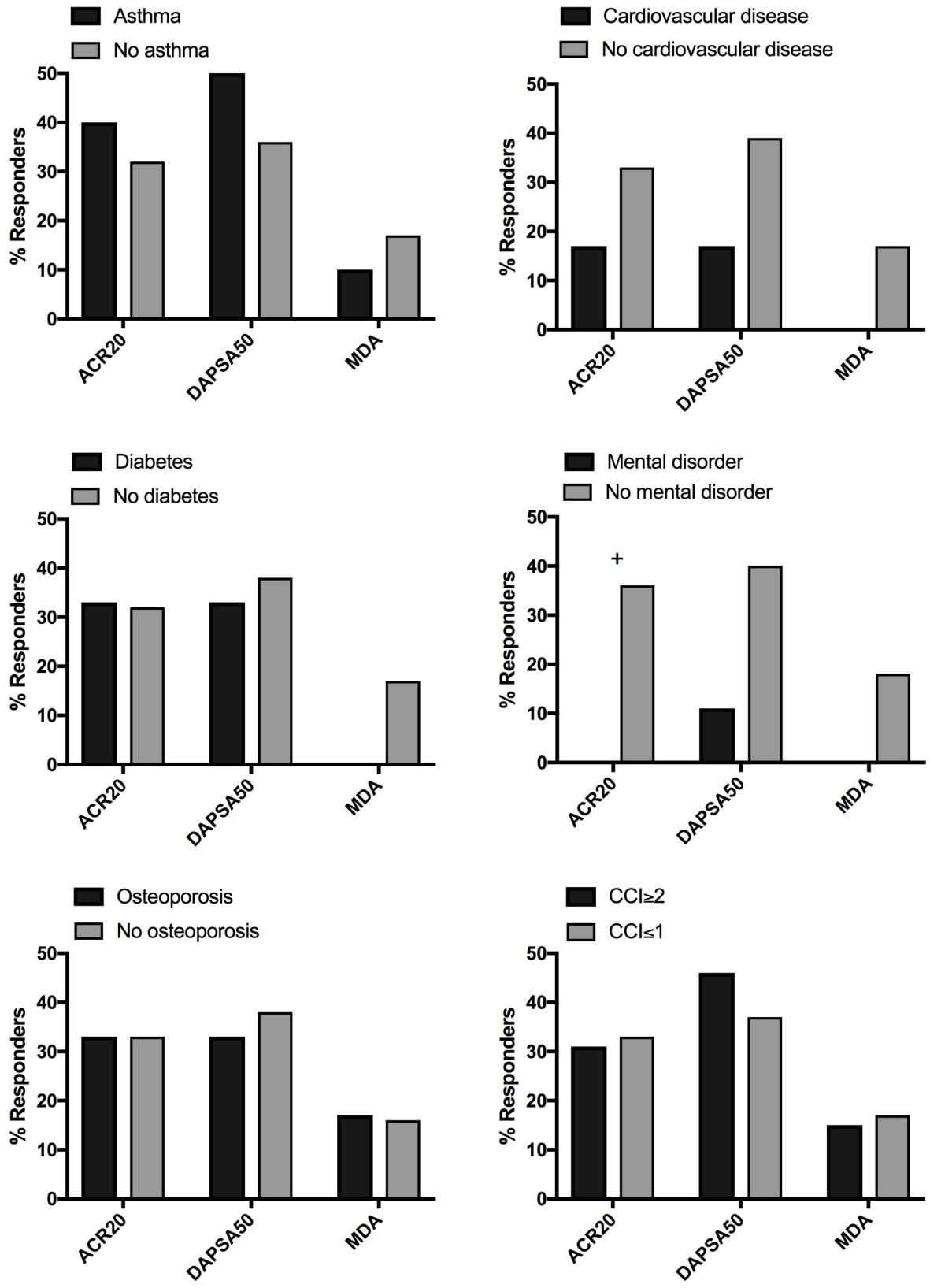

Psoriasis patients screened for eligibility[1] (n = 39)
Exclusion (n = 16)
Did not meet inclusion criteria (n = 9)[3]
Declined to participate (n = 7)
Psoriasis patients assessed for eligibility[2] (n = 23)
Exclusion (n = 3)
Did not meet inclusion criteria (n = 3)[4]
Inclusion (n = 20)

Figure S3.


Asthma
No asthma
% Responders
50
40
30
20
10
0
ACR20
DAPSA50
MDA
Cardiovascular disease
No cardiovascular disease
% Responders
50
40
30
20
10
0
ACR20
DAPSA50
MDA
Diabetes
No diabetes
% Responders
50
40
30
20
10
0
ACR20
DAPSA50
MDA
Mental disorder
No mental disorder
+
% Responders
50
40
30
20
10
0
ACR20
DAPSA50
MDA
Osteoporosis
No osteoporosis
% Responders
50
40
30
20
10
0
ACR20
DAPSA50
MDA
CCI≥2
CCI≤1
% Responders
50
40
30
20
10
0
ACR20
DAPSA50
MDA

Supplementary Table S1. Number of patients achieving ACR20, DAPSA50 and MDA according to comorbidity.

		ACR20		DAPSA50		MDA	
	n*	**Responders (n, %)**	**p**	**Responders (n, %)**	**p**	**Responders (n, %)**	**p**
Asthma	10	4 (40)	0.72	5 (50)	0.49	1 (10)	0.99
No asthma	89	28 (32)		32 (36)		15 (17)	
CVD	6	1 (17)	0.66	1 (17)	0.41	0 (0)	0.59
No CVD	93	31 (33)		36 (39)		16 (17)	
Diabetes	6	2 (33)	0.99	2 (33)	0.99	0 (0)	0.59
No diabetes	93	30 (32)		35 (38)		16 (17)	
Mental disorder	9	0 (0)	**0.029**	1 (11)	0.15	0 (0)	0.35
No mental disorder	90	32 (36)		36 (40)		16 (18)	
Osteoporosis	6	2 (33)	0.99	2 (33)	0.99	1 (17)	0.99
No osteoporosis	93	30 (33)		35 (38)		15 (16)	
CCI ≥2	13	4 (31)	0.99	6 (46)	0.55	2 (15)	0.99
CCI ≤1	87	29 (33)		32 (37)		15 (17)	

Responses are intention-to-treat (ITT). p values <0.05 are marked with bold. ACR20, American College of Rheumatology 20% improvement criteria; DAPSA50, 50% improvement in Disease Activity index for PSoriatic Arthritis; MDA, Minimal Disease Activity; CCI, Charlson Comorbidity Index; CVD, cardiovascular disease. *One patient did not provide information on presence or absence of current comorbidities at baseline, but the patient did participate in the laboratory and clinical assessments including assessment of CCI score.

Supplementary Table S2. Core Outcome Set measurements at baseline and 4-months follow-up according to asthma and cardiovascular disease (CVD) at baseline.

	Baseline			Follow-up		
	Asthma (n = 10)	**No asthma (n = 89)**	**p**	**Asthma (n = 10)**	**No asthma (n = 89)**	**p**
MSK disease activity						
SJC (66)	8 (6-11)	5 (2-8)	0.11	3 (2-6)	2 (1-6)	0.54
TJC (68)	18 (14-23)	14 (6-27)	0.16	9 (6-23)	7 (3-17)	0.32
SPARCC enthesitis	5 (5-6)	4 (2-7)	0.27	6 (1-7)	4 (1-6)	0.58
Skin disease						
PASI	0.4 (0.0-5.4)	1.3 (0.3-4.5)	0.31	1 (0.6-1.4)	0.5 (0.0-1.6)	0.40
Pain						
VAS pain	67 (33-75)	59 (28-72)	0.53	59 (14-74)	36 (12-64)	0.44
SF36 Bodily Pain	36 (22-51)	41 (22-61)	0.43	47 (31-74)	52 (41-74)	0.46
Physical function						
SF-36 PF	45 (25-60)	60 (45-80)	**0.015**	58 (25-70)	70 (50-85)	0.069
HAQ-DI	1.32 (0.75-1.88)	0.88 (0.38-1.25)	0.047	0.94 (0.50-1.75)	0.50 (0.25-1.00)	**0.038**
Health related QoL						
DLQI	1 (1-6)	1 (0-4)	0.54	1 (1-6)	1 (0-2)	0.18
PsAID-9	5.5 (3.9-6.4)	5.1 (3.0-6.5)	0.45	4.3 (1.7-4.7)	3.6 (1.5-5.6)	0.53
Patient Global						
Patient Global VAS	73 (59-80)	63 (35-79)	0.26	66 (13-80)	47 (11-66)	0.37
Fatigue						
NRS Fatigue	7 (5-8)	6 (3-8)	0.70	5 (2-8)	5 (1-6)	0.74
SF-36 Vitality Scale	30 (10-50)	35 (25-60)	0.15	35 (25-55)	50 (30-70)	0.20
Systemic inflammation						
CRP (mg/L)	2 (1-4)	4 (1-10)	0.34	2 (1-4)	3 (1-6)	0.90
	CVD (n = 6)	**No CVD (n = 93)**	**p**	**CVD (n = 6)**	**No CVD (n = 93)**	**p**
MSK disease activity						
SJC (66)	9 (6-12)	5 (2.5-8)	0.056	7 (5-11)	2 (1-5)	**0.008**
TJC (68)	17.5 (6-50)	14 (7-26)	0.54	9.5 (6-38)	7 (2.5-16.5)	0.29
SPARCC enthesitis	4 (2-6)	4 (2-7)	0.95	3.5 (2-6)	4 (1-6)	0.67
Skin disease						
PASI	0.9 (0.6-3.4)	1.2 (0.3-4.8)	0.94	1.5 (0.9-3.4)	0.45 (0.0-1.5)	0.10
Pain						
VAS pain	65 (24-70)	59 (28-72)	0.90	64 (24-72)	36 (12-65)	0.22
SF36 Bodily Pain	51 (41-62)	41 (22-52)	0.18	51 (41-62)	52 (41-74)	0.84
Physical function						
SF-36 PF	77.5 (60-90)	55 (45-75)	0.15	82.5 (60-90)	70 (50-85)	0.36
HAQ-DI	0.63 (0.13-1.00)	0.88 (0.38-1.25)	0.37	0.63 (0.13-1.00)	0.63 (0.25-1.00)	0.89
Health related QoL						
DLQI	0.5 (0.0-6.0)	1.0 (0.0-4.0)	0.41	0.5 (0.0-1.0)	1.0 (0.0-3.0)	0.48
PsAID-9	5.0 (1.2-5.8)	5.2 (3.0-6.5)	0.55	4.4 (1.3-5.3)	3.6 (1.6-5.6)	0.68
Patient Global						
Patient Global VAS	64.5 (16-79)	64 (38-80)	0.64	61 (22-70)	47 (10-67)	0.45
Fatigue						
NRS Fatigue	7 (2-8)	6 (4-8)	0.70	5.5 (2-8)	5 (2-8)	0.76
SF-36 Vitality Scale	45 (25-80)	35 (25-55)	0.59	57.5 (45-75)	45 (30-65)	0.33
Systemic inflammation						
CRP (mg/L)	2 (1-2)	4 (1-10)	0.26	2 (1-2)	3 (1-6)	0.29

Values are intention-to-treat (ITT) and presented as median (interquartile range). p values <0.05 are marked with bold. MSK, musculoskeletal disease; SJC, swollen joint count; TJC, tender joint count; SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index; PASI, Psoriasis Area Severity Index; VAS, visual analogue scale; PF, physical function; SF-36, Short-form 36 questionnaire; HAQ-DI, Health Assessment Questionnaire Disability Index; QoL, quality of life; DLQI, Dermatology Life Quality Index; PsAID, Psoriatic Arthritis Impact of Disease; NRS, numerical rating scale; CRP, C-reactive protein.

Supplementary Table S3. Core Outcome Set measurements at baseline and 4-months follow-up according to diabetes and mental disorders at baseline.

	Baseline			Follow-up		
	Diabetes (n = 6)	**No diabetes (n = 93)**	**p**	**Diabetes (n = 6)**	**No diabetes (n = 93)**	**p**
MSK disease activity						
SJC (66)	5 (3-6)	6 (3-9)	0.61	2.5 (1-5)	2.5 (1-6)	0.95
TJC (68)	16 (7-25)	14 (7-27)	0.87	8.5 (7-25)	7 (2.5-16.5)	0.39
SPARCC enthesitis	5 (2-7)	4 (2-7)	0.88	3 (0-9)	4 (1-6)	0.87
Skin disease						
PASI	5.1 (1.0-13.5)	1.2 (0.3-4.1)	0.20	4.6 (0.7-8.3)	0.6 (0.0-1.5)	0.15
Pain						
VAS pain	58 (50-72)	59 (28-72)	0.54	55 (50-73)	34 (12-67)	0.22
SF36 Bodily Pain	31 (31-51)	41 (22-52)	0.49	41 (31-52)	52 (41-74)	0.27
Physical function						
SF-36 PF	30 (20-40)	60 (45-75)	**0.009**	38 (30-50)	70 (55-85)	**0.004**
HAQ-DI	1.25 (1.00-1.63)	0.88 (0.38-1.25)	0.11	1.25 (1.00-1.50)	0.50 (0.25-1.00)	0.059
Health related QoL						
DLQI	1 (1-4)	1 (0-5)	0.90	1 (1-4)	1 (0-2)	0.52
PsAID-9	6.1 (4.7-6.5)	5.1 (3.0-6.5)	0.32	4.4 (3.5-5.0)	3.6 (1.5-5.6)	0.47
Patient Global						
Patient Global VAS	68 (63-89)	63 (35-79)	0.29	63 (43-90)	47 (11-68)	0.18
Fatigue						
NRS Fatigue	6 (5-8)	6 (4-8)	0.77	5 (3-6)	5 (2-8)	0.98
SF-36 Vitality Scale	33 (25-35)	35 (25-60)	0.53	30 (25-65)	50 (30-70)	0.45
Systemic inflammation						
CRP (mg/L)	78 (4-10)	4 (1-9)	0.14	4 (2-6)	2 (1-5)	0.39
	Mental disorder (n = 9)	**No mental disorder (n = 90)**	**p**	**Mental disorder (n = 9)**	**No mental disorder (n = 90)**	**p**
MSK disease activity						
SJC (66)	1 (0-3)	6 (3-9)	**0.006**	0 (0-7)	3 (1-5)	0.36
TJC (68)	25 (9-37)	14 (7-25)	0.52	25 (3-33)	7 (3-14)	**0.061**
SPARCC enthesitis	5 (4-9)	4 (2-7)	0.23	9 (5-10)	4 (1 -6)	**0.025**
Skin disease						
PASI	0.9 (0.6-6.2)	1.2 (0.3-4.1)	0.83	1.4 (0.5-2.1)	0.5 (0.0-1.5)	0.11
Pain						
VAS pain	72 (60-72)	53.5 (27-71)	**0.076**	71 (53-85)	34 (12-64)	**0.028**
SF36 Bodily Pain	31 (22-41)	41 (22-52)	0.24	41 (31-51)	52 (41-82)	**0.032**
Physical function						
SF-36 PF	50 (40-60)	60 (45-75)	0.21	60 (50-65)	70 (50-85)	0.17
HAQ-DI	1.00 (0.75-1.25)	0.88 (0.38-1.25)	0.53	1.00 (0.75-1.00)	0.50 (0.25-1.00)	0.15
Health related QoL						
DLQI	2 (1-6)	1 (0-4)	0.15	3 (2-4)	1 (0-2)	**0.023**
PsAID-9	6.5 (5.4-7.1)	5.0 (2.9-6.3)	0.064	6.5 (5.0-7.1)	3.4 (1.5-5.1)	**0.006**
Patient Global						
Patient Global VAS	77 (70-89)	62.5 (34-79)	**0.028**	80 (43-88)	44.5 (10-66)	**0.020**
Fatigue						
NRS Fatigue	8 (6-8)	6 (3-8)	0.17	8 (8-8)	5 (2-7)	**0.001**
SF-36 Vitality Scale	25 (20-30)	35 (25-60)	0.075	25 (20-45)	50 (30-70)	**0.011**
Systemic inflammation						
CRP (mg/L)	6 (1-6)	4 (1-11)	0.81	2 (1-3)	3 (1-6)	0.40

Values are intention-to-treat (ITT) and presented as median (interquartile range). p values <0.05 are marked with bold. MSK, musculoskeletal disease; SJC, swollen joint count; TJC, tender joint count; SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index; PASI, Psoriasis Area Severity Index; VAS, visual analogue scale; PF, physical function; SF-36, Short-form 36 questionnaire; HAQ-DI, Health Assessment Questionnaire Disability Index; QoL, quality of life; DLQI, Dermatology Life Quality Index; PsAID, Psoriatic Arthritis Impact of Disease; NRS, numerical rating scale; CRP, C-reactive protein.

Supplementary Table S4. Core Outcome Set measurements at baseline and 4-months follow-up according to osteoporosis and Charlson Comorbidity Index (CCI) at baseline.

	Baseline			Follow-up		
	Osteoporosis (n = 6)	**No osteoporosis (n = 93)**	**p**	**Osteoporosis (n = 6)**	**No osteoporosis (n = 93)**	**p**
MSK disease activity						
SJC (66)	8 (4-11)	5 (3-8)	0.22	4 (3-6)	2 (1-6)	0.20
TJC (68)	25 (17-37)	14 (7-27)	0.12	9 (7-25)	7 (3-17)	0.44
SPARCC enthesitis	5 (4-6)	4 (2-7)	0.72	3 (1-5)	4 (1-7)	0.41
Skin disease						
PASI	3.4 (0.6-6.2)	1.2 (0.3-4.1)	0.46	0.6 (0.4-3.4)	0.6 (0.0-1.5)	0.51
Pain						
VAS pain	62.5 (24-73)	59 (28-72)	0.87	57 (24-73)	36 (12-67)	0.39
SF36 Bodily Pain	46 (41-52)	41 (22-52)	0.53	47 (41-61)	52 (41-74)	0.71
Physical function						
SF-36 PF	58 (50-60)	60 (40-75)	0.98	58 (50-85)	70 (50-85)	0.67
HAQ-DI	0.88 (0.63-1.25)	0.88 (0.38-1.25)	0.83	0.88 (0.38-1.00)	0.63 (0.25-1.00)	0.44
Health-related QoL						
DLQI	4 (0-6)	2 (0-4)	0.78	1 (0-5)	1 (0-2)	0.79
PsAID-9	5.7 (4.4-6.1)	5.1 (3.0-6.5)	0.78	4.7 (1.7-6.1)	3.6 (1.5-5.4)	0.47
Patient Global						
Patient Global VAS	62 (50-76)	64 (37-80)	0.73	56 (11-76)	47 (11-68)	0.87
Fatigue						
NRS Fatigue	7 (4-8)	6 (4 -8)	0.94	7 (2-8)	5 (2-8)	0.56
SF-36 Vitality Scale	40 (30-50)	35 (25-60)	0.57	40 (35-45)	50 (30-70)	0.71
Systemic inflammation						
CRP (mg/L)	1 (1-3)	4 (1-10)	0.11	1 (1-3)	3 (1-6)	0.19
	CCI ≥2 (n = 13)	**CCI ≤1 (n = 87)**	**p**	**CCI ≥2 (n = 13)**	**CCI ≤1 (n = 87)**	**p**
MSK disease activity						
SJC (66)	6 (4-8)	5 (2-9)	0.68	5 (1-8)	2 (1-5)	0.33
TJC (68)	23 (12-27)	14 (6-27)	0.16	9 (7-12)	7 (3-18)	0.56
SPARCC enthesitis	5 (3-7)	4 (2-7)	0.28	2 (0-6)	4 (1-6)	0.52
Skin disease						
PASI	1.9 (0.6-6.2)	1.2 (0.3-4.1)	0.51	1.0 (0.0-4.5)	0.6 (0.0-1.5)	0.50
Pain						
VAS pain	50 (27-83)	59.0 (28-72)	0.77	56 (24-73)	34 (11-65)	0.19
SF36 Bodily Pain	41 (31-51)	41.0 (22-52)	0.55	51 (31-61)	52 (41-82)	0.27
Physical function						
SF-36 PF	35 (25-60)	60.0 (45-75)	**0.040**	55 (30-70)	70 (55-85)	**0.047**
HAQ-DI	1.00 (0.63-1.63)	0.88 (0.38-1.25)	0.38	1.00 (0.38-1.50)	0.50 (0.25-1.00)	**0.038**
Health-related QoL						
DLQI	1 (0-3)	1 (0-5)	0.44	1 (1-3)	1 (0-2)	0.36
PsAID-9	5.8 (4.1-6.5)	5.2 (3.0-6.5)	0.46	4.1 (3.2-6.5)	3.5 (1.3-5.5)	0.21
Patient Global						
Patient Global VAS	72 (50-80)	63.0 (37-80)	0.50	61 (11-80)	43 (11-67)	0.33
Fatigue						
NRS Fatigue	6 (4-8)	6 (3-8)	0.49	5 (3-8)	5 (2-8)	0.91
SF-36 Vitality Scale	35 (25-45)	35 (25-60)	0.66	40 (25-55)	50 (30-70)	0.48
Systemic inflammation						
CRP (mg/L)	2 (1-10)	4 (1-10)	0.65	2 (1-6)	3 (1-6)	0.71

Values are intention-to-treat (ITT) and presented as median (interquartile range). p values <0.05 are marked with bold. MSK, musculoskeletal disease; SJC, swollen joint count; TJC, tender joint count; SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index; PASI, Psoriasis Area Severity Index; VAS, visual analogue scale; PF, physical function; SF-36, Short-form 36 questionnaire; HAQ-DI, Health Assessment Questionnaire Disability Index; QoL, quality of life; DLQI, Dermatology Life Quality Index; PsAID, Psoriatic Arthritis Impact of Disease; NRS, numerical rating scale; CRP, C-reactive protein.

Supplementary Table S5. Characteristics of patients reporting treatment of current mental disorders.

	Patients reporting current treatment of mental disorders		
	Yes (n = 9)	**No (n = 90)**	**p**
SJC (66)	1 (0-3)	6 (3-9)	**0.006**
TJC (68)	25 (9-37)	14 (7-25)	0.52
SPARCC (0–16)	5 (4-9)	4 (2-7)	0.23
TPC (0 – 18)	7 (4-9)	2 (0-5)	**0.046**
GAD-10 (0 – 50)	18.0 (15.0-22.0)	6.5 (4.0-11.0)	**<0.001**
SF-36 MH (0 – 100)*	36 (28-60)	76 (60-88)	**0.003**
SF-36 MCS (0 – 100)*	33.7 (25.5-44.5)	52.1 (41.1-58.1)	**0.008**

Values are the median (interquartile range). p values <0.05 are marked with bold. SJC, swollen joint count; TJC, tender joint count; SPARCC, Spondyloarthritis Research Consortium of Canada enthesitis index; TPC, tender point coint; GAD-10, Generalized Anxiety Disorder questionnaire; SF-36, Short Form 36 questionnaire; MH, mental health; MCS, mental component summary. *Higher scores indicate better health status.

Supplementary Table S6. Treatment specification according to comorbidity.

	Obesity (n = 22)	Non-obese (n = 77)	p	Hypertension (n = 29)	No hypertension (n = 70)	p
bDMARD naïve	15 (68)	58 (75)	0.50	22 (76)	51 (72)	0.76
No. of previous bDMARDs			0.58			0.17
1	2 (9)	10 (13)		1 (3)	11 (16)	
2	2 (9)	3 (4)		1 (3)	4 (6)	
3	1 (5)	3 (4)		2 (7)	2 (3)	
4	2 (9)	3 (4)		3 (11)	2 (3)	
csDMARD initiator	8 (36)	36 (47)	0.39	14 (48)	30 (43)	0.62
bDMARD initiator	14 (64)	41 (53)	0.39	15 (52)	40 (57)	0.62
Current prednisolone	1 (5)	13 (17)	0.18	4 (14)	10 (14)	0.99
NSAIDs			0.11			0.61
<4 days per week	12 (54)	56 (73)		21 (72)	47 (67)	
4 to 7 days per week	10 (46)	21 (27)		8 (28)	23 (33)	
Mild analgesics*			**<0.001**			0.20
<4 days per week	7 (32)	57 (74)		16 (55)	48 (69)	
4 to 7 days per week	15 (68)	20 (26)		13 (45)	22 (31)	
Opioids			0.18			**0.022**
<4 days per week	19 (86)	73 (95)		24 (83)	68 (97)	
4 to 7 days per week	3 (14)	4 (5)		5 (17)	2 (3)	
Treatment for psoriasis**	4 (18)	29 (38)	0.087	9 (31)	24 (34)	0.76

Values are number of patients (percentages). P values <0.05 are marked with bold. P values were calculated by use of Pearson's chi-squared test if number of expected values in any of the cells of the contingency table was ≥5, otherwise we used Fisher's exact test. bDMARD, biological disease modifying anti-rheumatic drugs; csDMARD, conventional synthetic DMARD, NSAID, nonsteroidal anti-inflammatory drug. *Includes paracetamol and acetylsalicylic acid. **Includes topical treatment and/or phototherapy.

Supplementary Table S7. Treatment specification according to comorbidity.

	WP (n = 23)	No WP (n = 77)	p	CCI ≥1 (n = 35)	CCI = 0 (n = 65)	p
bDMARD naïve	15 (65)	58 (75)	0.34	24 (68)	49 (75)	0.46
No. of previous bDMARDs			0.58			0.93
1	3 (13)	9 (12)		6 (17)	6 (9)	
2	2 (9)	4 (5)		0 (0)	6 (9)	
3	2 (9)	2 (3)		3 (9)	1 (2)	
4	1 (4)	4 (5)		2 (6)	3 (5)	
csDMARD initiator	8 (35)	36 (47)	0.31	16 (46)	28 (43)	0.80
bDMARD initiator	15 (65)	41 (53)	0.31	19 (54)	37 (57)	0.80
Current prednisolone	2 (9)	12 (16)	0.52	3 (9)	11 (17)	0.37
NSAIDs			0.14			0.95
<4 days per week	13 (56)	56 (73)		24 (69)	45 (69)	
4 to 7 days per week	10 (44)	21 (27)		11 (31)	20 (31)	
Mild analgesics*			**0.001**			**0.011**
<4 days per week	8 (35)	57 (74)		17 (49)	48 (74)	
4 to 7 days per week	15 (65)	20 (26)		18 (51)	17 (26)	
Opioids			0.20			**0.049**
<4 days per week	20 (87)	73 (95)		30 (86)	63 (97)	
4 to 7 days per week	3 (13)	4 (5)		5 (14)	2 (3)	
Treatment for psoriasis**	7 (30)	26 (34)	0.77	9 (26)	24 (37)	0.26

Values are number of patients (percentages). P values <0.05 are marked with bold. P values were calculated by use of Pearson's chi-squared test if number of expected values in any of the cells of the contingency table was ≥5, otherwise we used Fisher's exact test. bDMARD, biological disease modifying anti-rheumatic drugs; CCI, Charlson Comorbidity Index; csDMARD, conventional synthetic DMARD, NSAID, nonsteroidal anti-inflammatory drug; WP, widespread pain. *Includes paracetamol and acetylsalicylic acid. **Includes topical treatment and/or phototherapy.