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Title: An international multi-centre analysis of current prescribing practices and shared decision-making in Psoriatic Arthritis

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Authors contributions	<p>LW and CC wrote the initial draft of the manuscript.</p> <p>CW-S co-designed the statistical analysis and contributed to the methods and results of the manuscript.</p> <p>LC was chief investigator.</p> <p>The steering committee (LG, UK, EL, RQ) participated in designing the study, translated the documents, obtained the national ethical approvals and were national principal investigators.</p> <p>All other co-authors aided in data collection at individual centres.</p> <p>All authors read, contributed to and approved the final manuscript before submission.</p>
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Abstract: Max 350 words

Background: Psoriatic arthritis (PsA) is a multi-system disease with a range of treatment options. Shared decision-making (SDM) is advocated to improve patient outcomes. We aimed to analyse current prescribing practices and the extent of SDM in PsA consultations across Europe.

Methods: The ASSIST study was a cross-sectional observational study of PsA patients aged 18 years and older, attending a face-to-face appointment between July 2021 and March 2022. Patient demographics, current treatment and treatment decisions were recorded. The extent of SDM was measured by the clinician's effort to collaborate (CollaboRATE questionnaire) and patient's communication confidence (Perceived Efficacy in Patient-Physician Interactions tool, PEPPI-5).

Results: 503 patients were included from 24 centres across 5 countries (UK, France, Germany, Italy and Spain). Physician- and patient-reported measures of disease activity were highest in the UK, where median patient age was lowest. Conventional synthetic (cs) DMARDs constituted a higher percentage of current PsA treatment in UK than continental Europe (66.4% vs 44.9%), whereas biologic use was more frequent in Europe than the UK (68.1% vs 36.4%). Implementing a treatment change was most common in the UK, predominantly being a treatment increase. CollaboRATE and PEPPI-5 scores were high throughout, indicating high levels of clinician collaborative effort and patient communication confidence. Mean CollaboRATE and PEPPI scores in those with and without treatment escalation were similar. Of 16 patients with low CollaboRATE scores (<5), no patients with low PsAID-12 scores (<5) had treatment escalation. However, of 226 patients with high CollaboRATE scores, 59 patients with low PsAID-12 scores received treatment escalation.

Conclusions: Disease characteristics and treatment strategies varied by country. Higher rates of treatment escalation seen in the UK may be explained by higher disease activity and a younger cohort. High levels of patient-reported collaboration in face-to-face PsA consultations reflects effective implementation of the SDM approach in this field. Our data that, in patients with mild disease activity, only those with higher perceived collaboration underwent treatment escalation may reflect the role of SDM in eliciting otherwise undetected symptoms/concerns that influence treatment decisions.

Registration – NCT05171270

Keywords: Psoriatic arthritis; prescribing practices; shared decision-making; collaboration.

Background

Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy, affecting 20-30% of patients with psoriasis [1,2]. The condition has a heterogeneous phenotype, with inflammation affecting the joints, tendons, soft tissue, skin, nails and spine to differing extents between patients. PsA is associated with a reduced life expectancy and significant impact on quality of life through musculoskeletal symptoms and associated co-morbidities [3,4]. Multiple pharmacological treatment options exist, with significant developments in the field of disease-modifying antirheumatic drugs (DMARDs) in recent years [5]. There has been an expansion of treatment options beyond traditional conventional synthetic DMARDs (csDMARDs), such as methotrexate, sulfasalazine and leflunomide, to targeted therapies including i) biological agents (bDMARDs) that target underlying pathogenic molecules, such as tumour necrosis factor (TNF), interleukin (IL)-12/23, IL-23 and IL-17A/F, and ii) targeted synthetic DMARDs such as Janus kinases (JAKs) and phosphodiesterase-4 (PDE4). National and international guidelines have been developed to inform treatment decisions in PsA [6,7]. However, treatment decisions must be tailored to the individual, given the heterogeneity in clinical phenotype and the varying efficacy of each treatment on different disease domains. Treatment approaches are likely to vary by geographical location, driven by differences in healthcare services and reimbursement, but an observational analysis of current prescribing practices in PsA has not been undertaken.

Shared decision-making (SDM) is an important component of personalised healthcare, where treatment selection is guided by collaboration between the clinician and the patient to ensure the incorporation of patient priorities and values. SDM has been shown to improve outcomes and increase treatment compliance across multiple clinical groups [8-11]. It relies on both the clinician's effort to incorporate patient priorities and the patient's confidence in voicing their values. The CollaboRATE questionnaire and Perceived Efficacy in Patient-Physician Interactions (PEPPI-5) tool are patient-reported measures of the clinician's collaborative effort and patient communication confidence, respectively [12-15]. Despite SDM being a top international priority, there are no studies examining the degree of SDM in PsA consultations to date [16].

We undertook an international observational analysis to examine and compare current prescribing practices and SDM in PsA consultations across Europe.

Methods:

Study population and design

A subanalysis was undertaken using data from the international, cross-sectional study (ASSIST) to explore treatment decisions and SDM in adult PsA consultations across Europe. Patients aged 18 years and older attending a face-to-face rheumatology appointment at a specialist rheumatology centre between July 2021 and March 2022 were eligible for inclusion (NCT05171270). All patients had to have previously received a diagnosis of PsA by a rheumatologist according to the CLASSification of Psoriatic Arthritis criteria [17]. Patients were selected by systematic sampling, with a different random starting patient "number" per centre, from 24 centres across the UK, France, Germany, Italy, and Spain. The target was 100 patients per country and at least 15 per centre. Patients were not eligible for the study if they had a new diagnosis of PsA at the current clinic visit,

were not comfortable completing an app-based questionnaire or paper case-report form, or were unable to speak/read the local language.

Data

The following patient and disease characteristics were recorded: patient demographics, PsA duration, current treatment, number of comorbidities (according to the functional comorbidity index [18]) and disease activity. Disease components were measured by:

- i) A clinical assessment of tender and swollen joint count, dactylitis count, body surface area of psoriasis and physician numerical rating score (NRS) of overall disease activity.
- ii) Leeds Enthesitis Index (LEI) [19]
- iii) PsAID-12 questionnaire via the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) app on a tablet (scored from 0-10, with 10 reflecting worst possible health) [20]. The PsAID-12 score is a weighted sum of the scores for the 12 questions divided by 20.
- iv) Patient numerical rating scale (NRS) for global disease activity (psoriasis and arthritis) and pain (scored from 0-10, with 10 reflecting highest disease activity) [21]
- v) The health assessment questionnaire (HAQ, scored 0-3 with 3 being worst health) [22]
- vi) The EQ-5D VAS for current health (scored 0-100, with 100 being best possible health) [23].

Treatment decisions were documented as no change in treatment, treatment escalation or treatment reduction. Treatment escalation included dose increase, frequency increase, altered route of administration, medication addition or medication switch. The 3-item patient-reported CollaboRATE questionnaire and 5-item patient-reported Perceived Efficacy in Patient-Physician Interactions (PEPPI-5) tool were completed at the end of consultations, independent from clinicians [12,13, Supplementary 1]. The mean CollaboRATE score (mean score across 3 items) was recorded per patient. As the CollaboRATE score often shows ceiling effects, we also recorded whether patients providing the highest possible CollaboRATE score in all 3 items. The recorded PEPPI-5 score per patient is the sum of scores in the 5 items.

Statistical analysis

Descriptive statistics were calculated for patient demographics, disease activity, prescribing practices, CollaboRATE and PEPPI-5 scores across countries. Normally-distributed data with a low number of outliers is represented by mean and standard deviations. Skewed data or those with significant outliers are represented by median and IQR. Boxplots were created for physician NRS, PsAID-12 score, HAQ score, CollaboRATE and PEPPI-5 score by country. Returned questionnaires missing one or responses were excluded from analysis.

Results:

Demographic and clinical characteristics

Five hundred and three patients were recruited from 24 centres across the UK, Spain, France, Italy and Germany. Patient demographics varied by country (Table 1). Overall, 247 (49.1%) patients were female and mean patient age was 53 years (range 18-83). The UK had the lowest mean patient age, whilst Italy and France had a notably higher proportion of males. In all countries, the most common PsA subtype was peripheral arthritis (83.7% of all patients) and the number of co-morbidities was

low. Patient- and physician- markers of disease activity reflected mild disease across all countries (Table 1, Figure 1a-c), although median scores for tender joint counts, patient-reported and physician-reported disease activity, PsAID-12, EQ-VAS and HAQ were highest in the UK.

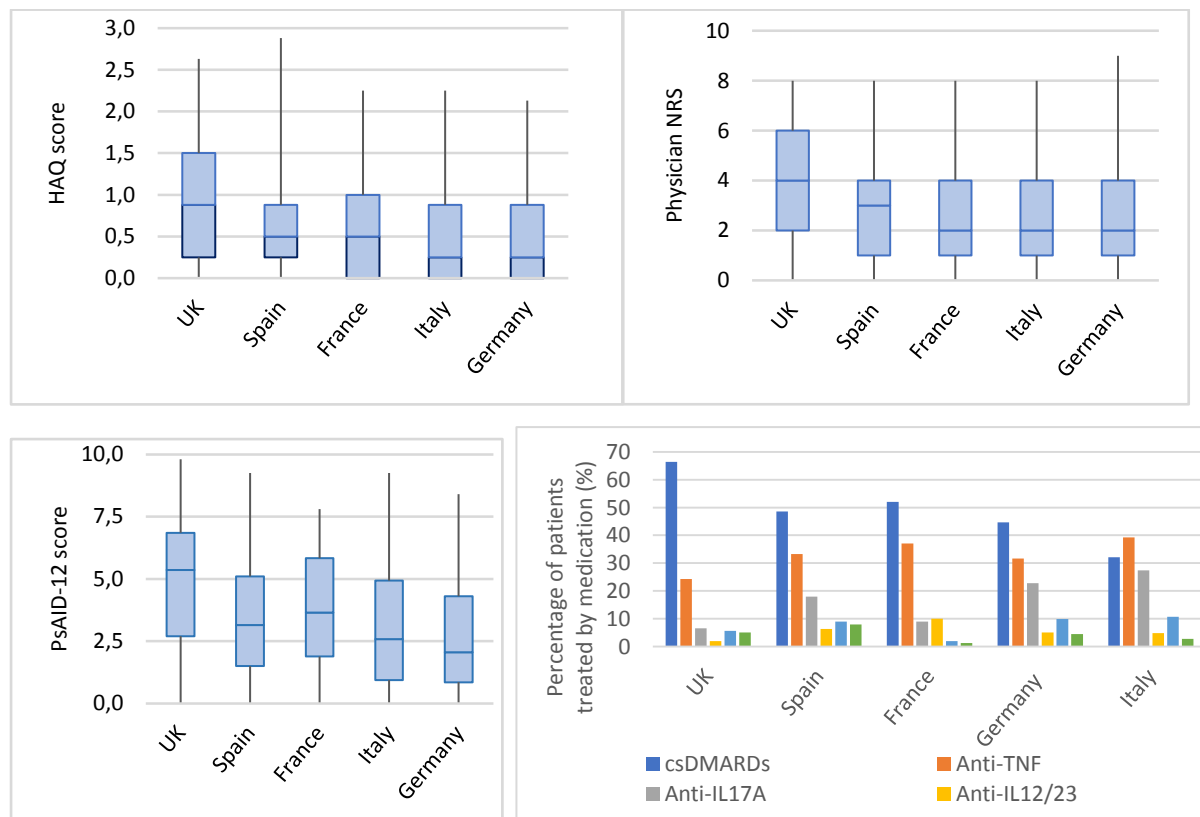


Figure 1. Box plots of disease activity, physical function and medication class by country (a) Physician NRS of overall global assessment (scored 0-10, with 10 as worst disease), (b) PsAID-12 score (scored 0-10, with 10 as worst disease) (c) Health Assessment Questionnaire (HAQ, scored 0-3 with 3 as worst health) and (d) medication class by country.

Prescribing practices

Current prescribing practices varied by country (Table 2). The use of glucocorticoids was uncommon across countries. CsDMARDs formed the predominant treatment in the UK (66.4% of UK patients) but were less frequently used in continental Europe (32.1-48.6% of patients per country). Conversely, bDMARDs were the most frequently used medication in all countries other than the UK. Among csDMARDs, the most commonly used medication in all countries was methotrexate (38.6% of all patients). The preference for bDMARD varied: adalimumab was the most used bDMARD in the UK and Spain; adalimumab and secukinumab were equally used in Germany; and ixekizumab and adalimumab were joint-first in Italy.

A decision to alter the current treatment regime occurred in 36.2% (182 patients) of the cohort, with treatment escalation being the predominant change (160 patients) (Table 3). Only 22 patients (4.4%) had their treatment decreased after their consultation. Notably, the frequency of treatment escalation was highest in the UK, occurring in nearly half of all UK consultations (51 patients, 47.7%), and lower in continental Europe (ranging from 23.8% to 31.5% per country). The predominant method to achieve treatment escalation was medication addition in all countries except Italy, where medication switch was most common.

Shared decision-making

CollaboRATE (n=498) and PEPPI-5 scores (n=494) were positively-skewed to the upper limit (Figure 2a-b, Table 3). 52.9% of all patients gave the highest possible CollaboRATE score. The mean PEPPI-5 score in male and female patients were similar (21.4 in both), as were the mean CollaboRATE scores (8.0 in both). When comparing patients with the lowest 5% of PEPPI-5 scores to the remaining cohort, the mean age (53.4 vs 54.0 years), percentage of female patients (58.3% vs 48.4%) and mean disease duration (11.2 vs 10.8 years) were similar.

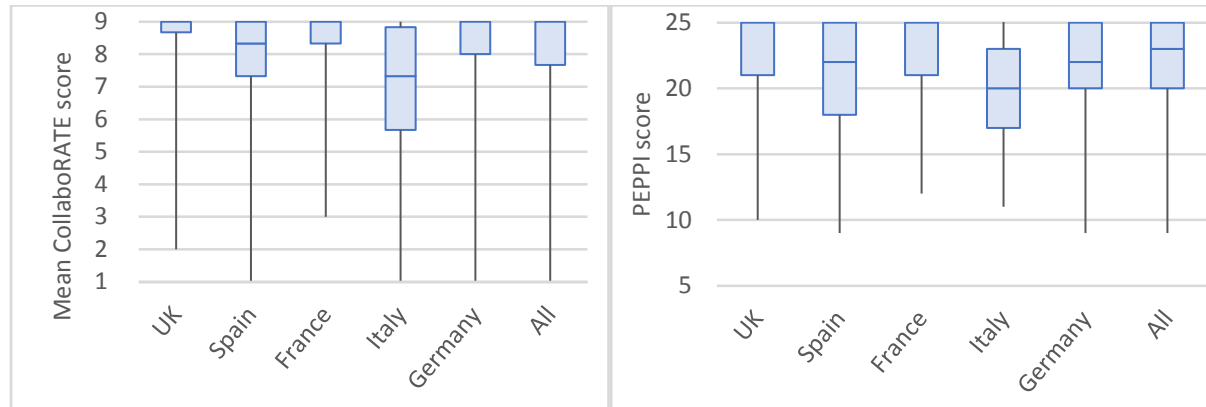


Figure 2 Box plots by country of (a) mean CollaboRATE score and (b) PEPPI-5 score.

There was no clear association between treatment escalation and CollaboRATE or PEPPI-5 scores: the mean CollaboRATE and PEPPI-5 scores were similar in those with and without treatment escalation (mean CollaboRATE 8.12 vs 7.88, mean PEPPI-5 21.3 vs 21.5) and the percentage of patients providing a maximum CollaboRATE score was similar irrespective of treatment escalation or not (51.9% vs 53.4%). The relationship between CollaboRATE, PsAID-12 and treatment escalation was examined (Figure 3). Of 16 patients with a low CollaboRATE score (CollaboRATE<4.5), treatment escalation only occurred in patients with a PsAID-12 >5 and not in any patients with PsAID-12 <5. In contrast, of 226 patients with CollaboRATE scores >4.5, treatment escalation occurred in patients with high and low PsAID-12 scores, including 59 patients with PsAID-12 <5.

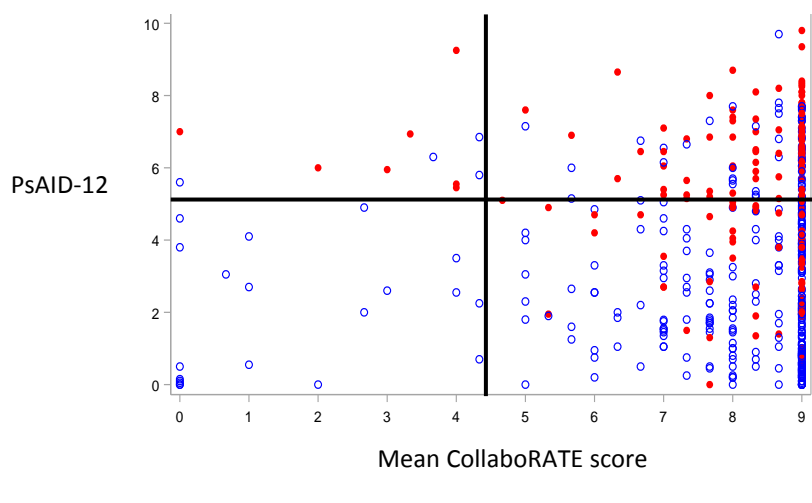


Figure 3. Treatment escalation (red) vs no escalation (blue), according to mean CollaboRATE and PsAID-12 scores per patient.

Discussion

The PsA cohort is highly heterogeneous in clinical phenotype and treatment responsiveness, making treatment decisions complex and multi-factorial [5]. Current prescribing practices are likely to vary by geographical location but this has not been well described. In this multi-centre international analysis of routine clinical practice, we found significant variation in prescribing practices by country. Notably, the frequency of bDMARD use in continental Europe was significantly higher than the UK, where csDMARD use predominated. National Institute for Health and Care Excellence (NICE) guidelines advise the use of at least 2 csDMARDs prior to starting biologic use in the UK and requires patients to have at least 3 tender and swollen joints, explaining the predominance of csDMARDs in the UK cohort [24]. In Europe, guidelines vary by country but the use of biologics is not generally restricted to a number of affected joints/enthesitis or a pre-requisite for failing 2 DMARDs [25-27]. The level of disease activity across multiple patient- and physician- reported outcome measures was highest in the UK, potentially reflecting current prescribing differences or a selection bias. The UK has 25% fewer physicians per 1000 people than mainland Europe [28]. Post-Covid clinical pressures in the UK during ASSIST recruitment meant that those attending a face-to-face consultation were those with active disease flares. A higher capacity to review stable/non-flaring patients in Europe may explain some of the geographical differences in disease severity and treatment choices between UK and mainland Europe. Treatment escalation was more common in the UK (47.7% of patients) than Europe (23.8- 31.5% of patients per country), in keeping with the higher level of physician- and patient- reported disease activity, the predominance of csDMARD use and the younger patient demographic in the UK, with treatment escalation being more likely earlier in the disease course.

SDM is crucial in PsA, given the variation of clinical phenotypes and treatment efficacies in different disease domains. SDM can also help overcome the discordance in assessment of disease activity by the patient and the clinician, which is particularly noted in mild disease [29]. Despite its importance, the extent of SDM in PsA has not been examined as of yet. We measured clinician collaborative effort and patient communication confidence with CollaboRATE and PEPPI-5 questionnaires [12,13]. Reassuringly, we found high CollaboRATE and PEPPI-5 scores across centres, irrespective of treatment decision. Patients were recruited by systematic sampling to minimise selection bias and questionnaires were completed independent from clinicians. These results differ from previous analyses of SDM which reported lower rates of SDM in other inflammatory arthropathies. A self-reported analysis of SDM amongst rheumatologists treating rheumatoid arthritis in Japan found only 27% practiced SDM and an independent observational analysis of recorded rheumatoid arthritis consultations in the Netherlands found a mean score of 28/100 on the observer patient involvement scale, an alternative measure of SDM [30,31]. The contrast with our findings may reflect an increased awareness of- and/or training in- SDM over recent years.

In consultations with lower levels of reported collaboration, treatment escalation was only seen in patients with higher disease impact (PsAID-12 score >5). However, in consultations with high levels of clinician effort to collaborate, treatment escalation occurred in patients with mild or active disease (low or high PsAID-12 scores). This may reflect improved identification of symptoms/concerns in more collaborative consultations that subsequently justify treatment escalation, underlining the importance of SDM. However, the data could be explained by

retrospective bias, where patients who receive treatment escalation are more likely to report their consultation as collaborative than those that don't.

Data generalisability was enhanced by undertaking an international analysis of over 500 participants, including multiple centres per country. However, all patients were recruited from specialist PsA clinics and disease activity was generally low, which may differ from other rheumatology clinics. Limitations of our study also include clinician awareness of SDM assessment, the ineligibility of patients who were unable to speak/read the local language and inclusion only of face-to-face consultations. With an increasing frequency of virtual consultations, it is important to assess whether high levels of SDM are maintained on online platforms. Future qualitative work to identify factors associated with more collaborative consultations may guide improvements in clinical practice.

Conclusion

This study delineates current PsA prescribing practices, disease characteristics and shared decision-making across multiple centres in the UK, France, Germany, Italy and Spain. Disease characteristics and treatment strategies varied between countries, but particularly between UK and mainland Europe. In keeping with a greater restriction on bDMARD use, csDMARDs predominated in the UK. Patients reported high levels of SDM in face-to-face PsA consultations, unrelated to treatment escalation. In patients with low PsAID-12 scores, those with higher perceived collaboration were more likely to have treatment escalation than those without, which may reflect the identification of otherwise undetected symptoms/concerns.

Supplementary material

Measures of shared decision-making.

CollaboRATE. Each of the following is scored from 0 (no clinician effort) to 9 (maximum clinician effort):

- i) How much effort was made to help you understand your health issues?
- ii) How much effort was made to listen to what matters most to you about your health issues?
- iii) How much effort was made to include what matters most to you in choosing what to do next?

PEPPI. Each of the following is scored from 1 (no confidence) to 5 (very confident):

- i) How confident are you in your ability to know what questions to ask a doctor?
- ii) To get a doctor to answer all of your questions?
- iii) To make the most of your visits with your doctors?
- iv) To get a doctor to take your chief health concern seriously?
- v) To get a doctor to do something about your chief health concern?

Tables

Table 1. Patient demographics and disease characteristics by country

	France (n=100)	Germany (n=101)	Italy (n=84)	Spain (n=111)	UK (n=107)	All (n=503)
Number of centres	5	5	4	5	5	24
Age in years, mean (S.D.)	54.9 (12.4)	55.3 (12.1)	54.3 (11.7)	53.8 (11.5)	51.6 (13.6)	53.9 (12.3)
Female sex, n (%)	47 (47.0)	58 (57.4)	29 (34.5)	54 (48.6)	59 (55.1)	247 (49.1)
Number of comorbidities, mean (S.D.)	1.5 (1.6)	1.4 (1.5)	1.2 (1.1)	1.3 (1.6)	1.5 (1.7)	1.4 (1.5)
Disease duration in years, mean (S.D.)	12.8 (9.6)	9.0 (8.5)	11.8 (11.2)	11.0 (8.7)	9.7 (8.3)	10.8 (9.3)
Disease subtype, n (%)						
Peripheral arthritis	72 (72.0)	84 (83.2)	73 (86.9)	91 (82.0)	101 (94.4)	421 (83.7)
Axial	21 (21.0)	11 (10.9)	5 (6.0)	15 (13.5)	4 (3.7)	56 (11.1)
Enthesitis	7 (7.0)	6 (5.9)	6 (7.1)	4 (3.6)	1 (0.9)	24 (4.8)

	France (n=100)	Germany (n=101)	Italy (n=84)	Spain (n=111)	UK (n=107)	All (n=503)
Tender joint count, median (IQR)	1.0 (0.0-4.0)	0.0 (0.0-3.0)	2.0 (0.0-5.0)	1.0 (0.0-4.0)	3.0 (0.0-9.0)	2.0 (0.0-4.0)
Swollen joint count, median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-1.0)	0.0 (0.0-2.0)	1.0 (0.0-3.0)	0.0 (0.0-1.0)
Dactylitis count, median (IQR)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)	0.0 (0.0-0.0)
Psoriasis body surface area, n (%)						
clear	37 (37.0)	39 (38.6)	28 (33.3)	37 (33.3)	34 (31.8)	175 (34.8)
<=3%	54 (54.0)	60 (59.4)	39 (46.4)	71 (64.0)	63 (58.9)	287 (57.1)
>3%	9 (9.0)	2 (2.0)	17 (20.3)	3 (2.7)	10 (9.3)	41 (8.2)
Leeds Enthesitis Score, n (%)						
0	70 (70.0)	86 (85.1)	54 (64.3)	81 (73.0)	68 (63.6)	359 (71.4)
1	5 (5.0)	5 (5.0)	10 (11.9)	7 (6.3)	12 (11.2)	39 (7.8)
2	15 (15.0)	6 (5.9)	7 (8.3)	10 (9.0)	12 (11.2)	50 (9.9)
3+	10 (10)	4 (4)	15 (17.)	13 (11.7)	15 (14.0)	55 (10.9)
Physician NRS of overall disease activity, median (IQR)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	2.0 (1.0-4.0)	3.0 (1.0-4.0)	4.0 (2.0-6.0)	3.0 (1.0-5.0)
Patient NRS of global disease activity, median (IQR)	3.7 (1.9-5.8)	2.0 (0.9-4.3)	2.6 (0.9-4.9)	3.3 (1.6-5.2)	5.4 (2.7-6.9)	3.5 (1.5-5.7)
Patient NRS of pain, median (IQR)	4.0 (2.0-6.5)	3.5 (1.5-6.0)	3.0 (1.0-7.0)	4.0 (2.0-6.5)	6.0 (3.0-7.5)	4.0 (2.0-7.0)
PsAID-12 score, median (IQR)	3.7 (1.8-5.5)	2.0 (0.9-4.0)	2.5 (0.8-5.0)	3.1 (1.5-5.0)	5.1 (2.4-6.7)	3.3 (1.3-5.4)

	France (n=100)	Germany (n=101)	Italy (n=84)	Spain (n=111)	UK (n=107)	All (n=503)
HAQ, median (IQR)	0.5 (0.0-1.0)	0.3 (0.0-0.9)	0.3 (0.0-0.9)	0.5 (0.3-0.9)	0.9 (0.3-1.5)	0.5 (0.0-1.0)
EQ-5D VAS for current health, median (IQR)	60 (50.0-80.0)	70.0 (42.5-85.0)	70.0 (50.0-80.0)	70.0 (55.0-80.0)	60.0 (40.0-75.0)	65.0 (50.0-80.0)

Table 2. Current prescribing practices and treatment decisions by country

	France (n=100)	Germany (n=101)	Italy (n=84)	Spain (n=111)	UK (n=107)	All (n=503)
Any csDMARDs, n (%)	52 (52.0)	45 (44.6)	27 (32.1)	54 (48.6)	71 (66.4)	249 (49.5)
Methotrexate	43 (43.0)	38 (37.6)	23 (27.4)	40(36.0)	50 (46.7)	194 (38.6)
Leflunomide	3 (3.0)	3 (3.0)	1 (1.2)	6 (5.4)	4 (3.7)	17 (3.4)
Sulfasalazine	0 (0.0)	0 (0.0)	4 (4.8)	6 (5.4)	19 (17.8)	29 (5.8)
Other	4 (4.0)	3 (3.0)	2 (2.4)	2 (1.8)	5 (4.7)	16 (3.2)
Any bDMARDs, n (%)	63 (63.0)	69 (68.3)	62 (73.8)	69 (62.2)	39 (36.4)	302 (60.0)
Anti-TNF	37 (37.0)	32 (31.7)	33 (39.2)	37 (33.3)	26 (24.3)	165 (32.8)
Anti-IL17A	9 (9.0)	23 (22.8)	23 (27.4)	20 (18.0)	7 (6.5)	82 (16.3)
Anti-IL12/23	10 (10.0)	5 (5.0)	4 (4.8)	7 (6.3)	2 (1.9)	28 (5.6)
Other	5 (5.0)	8 (7.9)	1 (1.2)	5 (4.5)	3 (2.8)	22 (4.4)
Oral glucocorticoids, n (%)	2 (2.0)	10 (9.9)	9 (10.7)	10 (9.0)	6 (5.6)	37 (7.4)
Treatment decisions, n (%)						
No change in treatment	70 (70.0)	67 (66.3)	60 (71.4)	72 (64.9)	52 (48.6)	321 (63.8)
Treatment Increase	28 (28.0)	26 (25.7)	20 (23.8)	35 (31.5)	51 (47.7)	160 (31.8)

Treatment Decrease	2 (2.0)	8 (7.9)	4 (4.8)	4 (3.6)	4 (3.7)	22 (4.4)
Treatment increase, n (%)						
Dose	8 (8.0)	4 (4.0)	3 (3.6)	7 (6.3)	8 (7.5)	30 (6.0)
Frequency	3 (3.0)	4 (4.0)	0 (0.0)	3 (2.7)	1 (0.9)	11 (2.2)
Route change	1 (1.0)	0 (0.0)	0 (0.0)	4 (3.6)	1 (0.9)	6 (1.2)
Additional medication	9 (9.0)	12 (11.9)	6 (7.1)	16(14.4)	28 (26.2)	71 (14.1)
Replacement medication	8 (8.0)	9 (8.9)	13 (15.5)	9 (8.1)	15 (14.0)	54 (10.7)

*Note that patients could have had more than one reason for increase/decrease so percentages may not sum to 100

Table 3. CollaborATE and PEPPi-5 scores by country

	France (n=100)	Germany (n=101)	Italy (n=84)	Spain (n=111)	UK (n=107)	All (n=503)
CollaborATE mean score, median (IQR)	9.0 (8.3-9.0)	9.0 (8.0-9.0)	7.3 (5.7-8.3)	8.3 (7.3-9.0)	9.0 (8.7-9.0)	9.0 (7.7-9.0)
CollaborATE maximum score, n (%)	70 (70.0)	55 (54.5)	21 (25.0)	49 (44.1)	71 (66.4)	266 (52.9)
PEPPi-5 total score, median (IQR)	25.0 (21.0-25.0)	22.0 (20.0-25.0)	20.0 (17.0-23.0)	22.0 (18.0-25.0)	25.0 (21.0-25.0)	23.0 (20.0-25.0)

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