

## Predictors of DAPSA28 remission in patients with psoriatic arthritis initiating a first TNF-inhibitor: results from 13 European registries

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## Abstract

### Objectives

In bio-naïve patients with Psoriatic arthritis (PsA) initiating a Tumour Necrosis Factor inhibitor (TNFi), we aimed to identify baseline predictors of Disease Activity index for PsA in 28 joints (DAPSA28) remission (primary objective) and DAPSA28 moderate response at 6 months, as well as drug retention at 12 months across 13 European registries.

### Methods

Baseline demographic and clinical characteristics were retrieved and the three outcomes investigated per registry and in pooled data, using logistic regression analyses on multiply imputed data. In the pooled cohort, selected predictors that were either consistently positive or negative across all three outcomes, were defined as common predictors.

### Results

In the pooled cohort (n=13,369), six-month proportions of remission, moderate response and 12-month drug retention were 25%, 34% and 63% in patients with available data (n=6,954, n=5,275 and n=13,369, respectively). Baseline predictors of remission, moderate response and 12-month drug retention were identified, five common across all three outcomes. Odds ratios (95% confidence interval) for DAPSA28 remission were: age, per year: 0.97 (0.96-0.98); disease duration, years (< 2 years as reference): 2-3 years: 1.20 (0.89-1.60), 4-9 years: 1.42 (1.09-1.84), ≥10 years: 1.66 (1.26-2.20); men vs. women: 1.85 (1.54-2.23); CRP >10 vs. ≤ 10 mg/l: 1.52 (1.22-1.89) and one mm increase in patient fatigue score: 0.99 (0.98-0.99).

### Conclusion

Baseline predictors of remission, response and adherence to TNFi were identified, of which five were common for all three outcomes, indicating that the predictors emerging from our pooled cohort may be considered generalisable from the country- to disease-level.

**Keywords:** Psoriatic arthritis, first TNF-inhibitor, predictors, DAPSA28, drug retention, real-world evidence

## Key messages

- This real-world study across 13 European countries presents data on 13,369 psoriatic arthritis (PsA) patients.
- Baseline predictors of remission, response and drug-retention following treatment with a first TNFi were identified.
- Consistency of predictors across registries and treatment outcomes, suggests generalisability from the country- to disease-level.

## INTRODUCTION

Tumor necrosis factor inhibitors (TNFi) have contributed to major improvements in clinical outcomes and quality of life for patients with psoriatic arthritis (PsA). However, many patients treated with TNFi fail to achieve the recommended treatment target of remission or, alternatively, low disease activity(1,2).

As the palette of treatment options continues to increase, understanding baseline determinants of a good response to TNFi is important for clinicians and patients in their shared decision-making. Several possible baseline predictors of treatment response in PsA have been investigated in individual countries or regions, including demographic, clinical, patient-reported and life-style characteristics, but no consistent pattern of predictors has emerged from the studies(3,4,13–17,5–12). Cross-country differences in baseline characteristics in PsA patients initiating TNFi treatment have been reported in a previous study from the EuroSpA collaboration(2), and such differences may have contributed to the inconsistencies in observed predictors of a treatment response across studies from individual countries.

In addition to differences in patient characteristics, a wide range of outcome measures has been applied(3,4,13–17,5–12), possibly reflecting the different views on how best to capture the full spectrum of PsA with its various clinical manifestations(18). In 2017, an international task force proposed the Disease Activity index for PSoriatic Arthritis (DAPSA)(19) for disease activity assessment in PsA(20). The DAPSA includes a 66/68 swollen/tender joint count, which, however, is not always performed in routine clinical settings. Therefore, the modified DAPSA28, based on a 28 joint count has been developed and compared to the original DAPSA and found valid (21). The

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4 authors suggested that DAPSA28 might be an alternative if the full DAPSA was missing in registry  
5 studies (21). While treatment responses according to DAPSA28 have been reported previously for  
6 14,261 European patients with PsA initiating a TNFi (2), predictors of such a response using  
7 DAPSA28 as outcome have not been investigated in a real-world cohort.  
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13 Thus, in this study of PsA patients starting their first TNFi, the primary aim was to identify baseline  
14 predictors of DAPSA28 remission after 6 months' treatment. Secondary aims were to identify  
15 baseline predictors of achieving DAPSA28 moderate response after 6 months and baseline  
16 predictors of 12-month drug retention.  
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## 20 21 22 **METHODS**

### 23 *Data sources*

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27 This study included secondary use of data on patients registered with a PsA diagnosis from 13  
28 European registries: ATTRA (Czech Republic), DANBIO (Denmark), ROB-FIN (Finland),  
29 ICEBIO (Iceland), GISEA (Italy), NOR-DMARD (Norway), Reuma.pt (Portugal), RRBR  
30 (Romania), biorx.si (Slovenia), BIOBADASER (Spain), SRQ (Sweden), SCQM (Switzerland) and  
31 TURKBIO (Turkey). In all registries, data are collected prospectively as part of routine clinical  
32 practice. Based on a predefined study protocol, anonymised data were uploaded by individual  
33 registries onto a secure central server.  
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### 39 *Patients and visits*

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42 Patients were included if they had a registered clinical diagnosis of PsA, were aged  $\geq 18$  years at  
43 diagnosis, and had initiated a first TNFi treatment at some point between diagnosis and 90 years of  
44 age, with a start date between January 1<sup>st</sup> 2009 and December 31<sup>st</sup> 2018. The baseline visit was  
45 defined as a registered visit within 30 days before to 30 days after the registered date of TNFi  
46 treatment start (i.e., baseline date), with priority given to visits before treatment start. The 6-month  
47 visit was defined as the one closest in time to 180 days within a range of 90 to 270 days after the  
48 baseline date. Baseline patient characteristics included demography, clinical measures, treatment  
49 and patient-reported outcomes (**table 1**).  
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## Endpoints

The primary endpoint was DAPSA28 remission (i.e. DAPSA28 $\leq$ 4) at 6 months on the first TNFi (21). Secondary endpoints were 1) DAPSA28 moderate response at 6 months (here defined as a 75% improvement from the baseline DAPSA28, similar to the corresponding response definition for the original DAPSA score, as no validated definition for DAPSA28 moderate response is available (22)) and 2) 12-month drug retention.

Patients with no available 6-month DAPSA28 data were classified as having achieved DAPSA28 remission and DAPSA28 moderate response, respectively, if they fulfilled both of the following two criteria: 1) they had stopped the TNFi before 6 months *and* no subsequent biological (b) or targeted synthetic (ts) disease-modifying anti-rheumatic drug (DMARD) was started within 6 months from the previous treatment start, *and* 2) if the clinician had stated “remission” as the reason for discontinuation (**figures 1a and b**). Patients who stopped the TNFi during the first 6 months due to lack of effect, were considered as *not* having achieved DAPSA28 remission or DAPSA28 moderate response. Patients discontinuing treatment due to AE, other reasons, or no stated reason, were not included in the analyses.

The 12-month drug retention was defined as the proportion of patients with a treatment duration  $\geq$  52 weeks. Treatment duration was defined as the number of weeks between the registered date of treatment start and the registered stop date. If the same drug was restarted within 3 months of a registered stop date, and no other treatment was recorded in between, the treatment periods were considered as one. Switch to a biosimilar of the same drug was disregarded. A treatment without a registered stop date was assumed to have been discontinued if a new b or ts DMARD treatment was recorded in the registry, and the stop date was then defined as the date of next treatment start. If no new treatment had been registered, a stop date was entered 12 months after the last registered visit. In the remaining observations, the stop date was defined as the date of data extraction, date of death, or end of registry follow-up, whichever came first.

## Ethics

All participating registries obtained necessary approvals from relevant authorities prior to data transfer to the EuroSpA coordinating center. This study was designed, implemented and reported in accordance with the Guidelines for Good Pharmacoepidemiology Practices (GPP) of the International Society for Pharmacoepidemiology (ISPE 2008), the STROBE (Strengthening the

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4 Reporting of Observational Studies in Epidemiology) guidelines(23) and the ethical principles laid  
5 down in the Declaration of Helsinki.

### 6 7 8 *Statistics*

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10 The statistical approach used for the current study has previously been applied in a cohort of  
11 patients with axial spondyloarthritis and is summarized below (24).

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13 Descriptive analyses of the baseline patient characteristics were performed per registry, in the  
14 pooled cohort, and additionally for patients with and without available data on DAPSA28 remission  
15 and moderate response at 6 months (in the pooled cohort only).

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17 Logistic regression analyses were used to identify baseline variables associated with the primary  
18 and secondary endpoints. Regression models were applied separately per registry and in the pooled  
19 cohort. Events-per-variable (EPV) was used to evaluate the sample size within the logistic  
20 regression models. Likelihood ratio tests were used to assess all models. Results of the multivariate  
21 models are presented as odds ratio (OR) with 95% or 85% confidence intervals (CI), see below.

### 22 23 24 25 26 27 28 29 *Independent variables*

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31 Sex, smoking status (current vs. previous/never), use of concomitant conventional synthetic (cs)  
32 DMARDs, C-reactive protein (CRP) ( $\leq 10$  vs.  $>10$  mg/l) and year of TNFi start (2009-2014 vs.  
33 2015-2018) were included as categorical variables. Age at treatment start, time since diagnosis,  
34 Body Mass Index (BMI), 28 tender and swollen joint counts, physician global score, Health  
35 Assessment Questionnaire (HAQ)(25), patient pain and fatigue scores were included as continuous  
36 variables. Age at diagnosis, erythrocyte sedimentation rate (ESR) and patient global score were not  
37 included in the models as they were considered to represent an overlap with time since diagnosis,  
38 CRP and patient pain and fatigue scores, respectively. For further details on independent variables,  
39 see **tables 2-5**.

### 40 41 42 43 44 45 46 47 48 *Missing data*

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50 Patients with no registration of concomitant csDMARDs were considered not using such drugs. For  
51 all remaining independent baseline variables, multiple imputation by chained equations (MICE) was  
52 applied in a pooled dataset containing all registries (30 imputed datasets).

### *Variable selection*

Variable selection in multiply imputed data for each endpoint followed. First, variable selection was performed separately in each of the 30 imputed datasets; the final model included the predictors that appeared in at least half of the models. Once the set of predictors was selected, the model was fitted to all imputed datasets and the model estimates were pooled according to Rubin's rules(24,26).

### *Analyses in individual registries*

To compare the selected predictors across registries, prediction models were first applied in each registry. A significance level of 0.157 was chosen due to small EPV values in some registries, corresponding to a 85% CI(27). The individual registry regression analyses were evaluated for consistency of selected predictors by visual inspection to determine if pooling of the data was feasible.

### *Analyses in the pooled cohort*

The pooled dataset was split into a derivation cohort and a validation cohort for each of the three endpoints, ensuring that 50% of patients from each registry went into each cohort, respectively. Registries with  $EPV \geq 1$  in the derivation cohort were pooled. Age, sex and registry were a priori forced into the models, and continuous variables were categorized if the assumption of linearity was violated. A significance level of 0.05 and a corresponding 95% CI was applied. Selected predictors that were either consistently positive or negative across all three outcomes, were defined as common predictors. The performance of the final multivariable models was evaluated in the validation cohorts by calculating the Area Under the Receiver Operating Curve (AUROC) (28).

### *Additional analyses*

In addition, we assessed whether differences in per registry proportions for DAPSA28 remission, moderate response and drug retention impacted the identified predictors, by stratifying the pooled cohort into three ordered levels based on visual inspection of the distribution of the outcomes in the registries. Prediction models were applied to each stratum, adjusting for registry using a variable selection process similar to the analyses in individual registries.

Finally, as DAPSA is the gold standard in the assessment of PsA patients, we conducted a prediction analysis in a subset with available remission and response criteria based on 66/68 joint counts, i.e. applying DAPSA remission ( $\leq 4$ ) and DAPSA moderate response (75% improvement



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4 from baseline) as outcomes and substituting the 28 joint counts with 66/68 joint counts as predictors  
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6 (22). R version 4.1.0 was used for statistical analyses.  
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## 8 **Results**

### 9 *Cohorts*

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11 Across the 13 registries, 13,369 PsA patients had started a first TNFi treatment during the study  
12  
13 period. Baseline patient characteristics by registry and pooled are shown in **table 1**, with  
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15 corresponding information on data availability in **Supplementary Table S1, available at**  
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17 ***Rheumatology online***. Numerical baseline differences between patients *with* versus *without* 6-  
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19 month follow-up data were only seen for concomitant csDMARD (**Supplementary Table S2,**  
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21 **available at *Rheumatology online***).  
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### 23 *DAPSA28 remission and moderate response*

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25 Of the 13 registries, 11 collected data on DAPSA28 (n=11,333) (**table 1**). A total of 6,442 (57%)  
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27 patients had a DAPSA28 assessment at 6-month follow-up visit after initiating their first TNFi, with  
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29 1,713 (27%) of these having achieved DAPSA28 remission. Of the 4,891 (43%) patients with no  
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31 DAPSA28 assessment at 6 months, 512 were instead classified according to their discontinuation  
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33 reason prior to 6 months follow-up (**figure 1a**). In total, 1,723 of 6,954 patients (25%) were  
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35 classified as having achieved DAPSA28 remission at 6 months. Proportions of DAPSA28 remission  
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37 ranged from 18% to 34% across registries (**table 2**). Corresponding results for DAPSA28 moderate  
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39 response are presented in **figure 1b** and **table 3**.  
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### 41 *Drug retention*

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43 All patients initiating a first TNFi were included in the drug retention analyses. Thereof, 8,461  
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45 (63%) were still on treatment at 12 months, with proportions ranging from 54% to 76% across  
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47 registries (**table 4**).  
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### 49 *Prediction analyses in individual registries*

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51 Eleven registries fulfilled the EPV criteria and were eligible for prediction analyses of the primary  
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53 endpoint DAPSA28 remission at 6 months. Male sex was identified as a predictor in 9 registries  
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55 (positive in 8 and negative in 1), while negative predictors included older age at treatment start (9  
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57 registries), higher tender joint count (7 registries), and higher BMI, patient pain and fatigue scores  
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59 in 5 registries. The remaining baseline variables were found predictive in less than half of the  
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4 eligible registries in which the variable was available, see **table 2** and **Supplementary Table S3**,  
5 **available at *Rheumatology* online**, for presentation of odds ratios (OR).  
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9 Eleven and 13 registries, respectively, were eligible for analyses of the secondary endpoints 6-  
10 month DAPSA28 moderate response and 12-month drug retention. Higher swollen joint count was  
11 identified as a positive predictor of DAPSA28 moderate response in 8 registries and CRP >10 mg/l  
12 in 6 registries. Negative predictors included older age at treatment start (6 registries) and current  
13 smoking, higher BMI and higher patient fatigue score (5 registries). Male sex and longer disease  
14 duration were positive predictors of 12-month drug retention in 10 and 8 registries, respectively,  
15 while TNFi start year 2015-2018 was a negative predictor in 10 registries. Concomitant csDMARD  
16 was a positive predictor in 6 and a negative predictor in 1 registry. The remaining baseline variables  
17 were found predictive in less than half of the registries in which the variable was available, see  
18 **table 3-4** and **Supplementary Tables S4-S5**, **available at *Rheumatology* online**, for presentation  
19 of ORs.  
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#### 28 *Prediction analyses in the pooled cohort*

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30 The consistency of predictors in the regression analyses per registry was found to justify pooling the  
31 data (**tables 2-4**). Common baseline predictors across all three outcomes (6-month DAPSA28  
32 remission/6-month DAPSA28 moderate response/12-month drug retention) in the derivation cohort  
33 were: male sex, longer disease duration, higher CRP (positive predictors); older age at treatment  
34 start, higher fatigue score (negative predictors) (**table 5**).  
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40 A higher pain score was a negative predictor of DAPSA28 remission and 12-month drug retention  
41 but a positive predictor of DAPSA28 moderate response (**table 5**).  
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44 The performance of the final models as assessed by the Area under the Receiver Operating Curve  
45 (AUROC) in the validation cohort was estimated to 0.75 (DAPSA28 remission), 0.73 (DAPSA28  
46 moderate response) and 0.64 (12-month drug retention), i.e. the models were able to correctly  
47 predict remission in 75%, moderate response in 73% and 12-month drug retention in 64% of  
48 patients (**table 5**).  
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53 In the pooled analyses *stratified* according to the proportion of patients achieving DAPSA28  
54 remission, DAPSA28 moderate response and 12-month drug retention, the common predictors  
55 identified in the pooled *unstratified* analyses (positive: male sex, longer disease duration, higher  
56 CRP; negative: older age at treatment start and higher patient fatigue score) were identified in at  
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4 least 2 of 3 strata across the three outcomes (**Supplementary Table S6, available at**  
5 ***Rheumatology online***).

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8 In the additional analyses with DAPSA remission and moderate response as outcomes, fewer data  
9 were available compared to the DAPSA28 analyses (**Supplementary Tables S1 and S7, available**  
10 **at *Rheumatology online***). Baseline differences between patients *with* versus *without* 6-month  
11 follow-up DAPSA were comparable with those seen in the DAPSA28 analyses, as were the  
12 predictors in the regression analyses per registry (data not shown). In the prediction models on  
13 pooled data, we identified the same predictors as for DAPSA28. In addition, 66 swollen joint count  
14 was a common positive predictor, which is in contrast to the DAPSA28 analyses, where 28 swollen  
15 joint count was not identified as a common predictor (**Supplementary Table S7**).

## 22 **Discussion**

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24 In this study, we identified five common baseline predictors of TNFi treatment response and  
25 retention, for the first time applying the DAPSA28 as endpoint in a large scale prediction analysis  
26 across 13 European countries through the EuroSpA collaboration.

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28 The main findings were that male sex, longer disease duration and higher CRP were positive  
29 predictors of DAPSA28 remission and DAPSA28 moderate response at 6 months and of drug  
30 retention after 12 months, while older age at treatment start and a higher patient fatigue score were  
31 negative predictors.

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33 In the EuroSpA collaboration, we have previously shown how baseline characteristics and treatment  
34 outcomes differ across European countries, possibly illustrating different prescription practices and  
35 access to therapy(2). To analyse if cross-country differences might contribute to inconsistencies in  
36 baseline predictors of treatment response across registries, we also stratified the pooled cohort by  
37 the proportion of patients achieving DAPSA28 remission, moderate response and 12-month drug  
38 retention, respectively, and identified baseline predictors for each stratum. We found that although  
39 the identified baseline predictors across strata and endpoints were not identical to the per-registry  
40 and unstratified pooled analyses, no major differences emerged. This suggests that despite the  
41 known and unknown differences across the individual countries, pooling of the cohorts to allow  
42 large scale analyses seems an acceptable approach. Thereby, the baseline predictors emerging from  
43 our pooled analyses may be considered generalizable from the country- to disease-level.

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4 We found that starting TNFi from 2015-2018 versus 2009-2014 reduced the chance of 12-month  
5 drug retention. This observed decrease in treatment retention over time may be explained by the  
6 emerging options for switching to another TNFi or a drug with a different mode of action, should  
7 the treatment target not be met. In support of this argument, a recent study on time trends in  
8 treatment response in European patients with PsA has indicated considerably longer drug retention  
9 rates prior to 2009(29).  
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15 A major strength of this study was the availability of similar clinical variables from 13 different  
16 European registries, allowing for the inclusion of the largest number of patients with PsA to date in  
17 a thorough analysis of baseline predictors of treatment response to TNFi. In previous similar  
18 studies, various outcome measures and baseline characteristics have been investigated, however few  
19 consistent predictors have emerged across the studies(3-7,13,14,16,17). Similarly, a meta-analysis  
20 from 2015 including 4034 patients with PsA identified several possible but no consistent predictors,  
21 which was ascribed to variation in the study design and heterogeneity in the treatment response  
22 measures used in the included studies(15).  
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30 In agreement with our findings, male sex has been suggested as a predictor for a good treatment  
31 response in other studies of patients with PsA(4,6,9,10,13,14). Similarly, our study adds weight to  
32 findings from previous smaller studies that have reported younger age at treatment start to be  
33 associated with better treatment responses(9,10,30). On the other hand, we found a positive  
34 association between longer disease duration at TNFi treatment start and both drug retention and  
35 treatment response. The patients with longer disease duration in our cohort had earlier onset PsA,  
36 which might also have contributed to the better outcomes, as there is evidence pointing towards a  
37 more aggressive disease course in PsA with onset later in life(31). Smaller studies have reported  
38 contradictory results regarding disease duration(16,17,32).  
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46 Higher CRP at baseline was, in our study, predictive of a good treatment response. In contrast,  
47 although CRP was included in many previous studies, it only predicted a good treatment response  
48 in a minority(3,9,12,17). Across those studies, the baseline level of inflammation, as assessed by the  
49 CRP was generally low, and the room for improvement therefore limited, which may potentially  
50 explain why this signal was not previously detected. It could also be an indication that many aspects  
51 besides inflammation play a role in this heterogeneous disease entity.  
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57 Baseline patient pain and fatigue scores were consistently associated with all treatment outcomes in  
58 our pooled cohort, with fatigue as a consistently negative predictor and pain as a negative predictor  
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4 of remission and drug retention but a positive predictor of DAPSA28 moderate response. Previous  
5 smaller studies have not found any clear pattern of associations between patient scores and  
6 treatment outcomes, but some have reported that worse scores at baseline predicted poorer  
7 outcomes(4,5,9,11–17). There is emerging evidence suggesting that the fatigue and pain  
8 experienced by patients may not be fully explained by the rheumatic disease. For example in a  
9 study of fatigue in PsA, inflammation, disease duration and chronic pain only explained two thirds  
10 of the experienced fatigue(33), and moreover, pain experienced by patients may be modulated by  
11 the concept of pain catastrophizing, a negative cognitive–affective response to anticipated or actual  
12 pain(34,35). Our findings may reflect such underlying mechanisms. Nevertheless, our findings  
13 suggest that the patient perspective is important for predicting the success of therapies, however,  
14 further investigation into the concepts of patient assessments is warranted.

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24 Functional disability measured by HAQ has previously been associated with poor outcomes in  
25 rheumatoid arthritis(36,37), but our results only showed a negative association with  
26 remission/response and not with drug retention. We find that the setting may not have been suitable  
27 for detecting such associations. For example, our patients have a relatively short disease duration  
28 and a high HAQ score may thus partly reflect reversible disease activity. In addition, drug retention  
29 is not a strictly clinical outcome measure and may be impacted by various factors not related to the  
30 disease status itself, i.e. treatment guidelines, access to drug, etc.

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37 Previously, other data on the use of csDMARDs in combination with TNFi suggested no additional  
38 effect of combination therapy on treatment response, but a possible beneficial effect on treatment  
39 retention(7,12,15,38–40). We have previously reported improved clinical response rates when  
40 combining adalimumab and infliximab but not etanercept with a csDMARD in PsA(41). In the  
41 current study, we were unable to replicate these findings as we analyzed TNFis as one group,  
42 however, our findings are in agreement with previous studies regarding drug retention.

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48 Cardiovascular risk factors, such as smoking and obesity, are overrepresented in patients with PsA  
49 compared to the general population(42,43), but the role of such factors during treatment with TNFi  
50 is unclear. In a few previous studies, smoking and obesity were associated with a poorer treatment  
51 response(4,7,13), while others found no such effect(10,14,16). In our pooled cohort, smoking was a  
52 negative predictor of DAPSA28 remission and drug retention but not associated with DAPSA28  
53 moderate response. Smoking was, however, negatively associated with DAPSA28 moderate  
54 response in half of the registries. Variation in smoking habits across countries in addition to  
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4 heterogeneity in the data collection, may play a role in the differences observed between the per  
5 registry and pooled analyses. BMI showed a similar tendency in our data, in line with our recent  
6 findings from a study on predictors of treatment response in axSpA(24).  
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10 Limitations to our study include its observational nature, which does not allow any causal  
11 conclusions to be drawn, and the lack of an endorsed PsA data collection framework limits  
12 generalizability of findings to this patient group. In addition, issues with data availability prompted  
13 us to use DAPSA28 over DAPSA although the latter is the gold standard in assessing PsA. We  
14 were, however, reassured in finding largely similar predictors in the subset of patients with  
15 available DAPSA scores. Selection bias based on availability of the DAPSA28 outcome cannot be  
16 ruled out, however, baseline characteristics for patients with and without available DAPSA28  
17 scores at follow-up were largely similar, and we therefore consider our findings to be generalizable.  
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25 In addition, we have previously discussed other limitations including the unbalanced sizes of the  
26 registries and missing data, which also apply to this study(24); moreover, we were not able to  
27 include psoriasis and other relevant comorbidities in the prediction models due to a lack of good  
28 quality data. Finally, we primarily investigated predictors of short- and medium-term outcomes,  
29 which is a limited window for a disease like PsA with fluctuating disease activity over time. An aim  
30 for future studies could be to investigate the maintenance of treatment responses within a longer  
31 time-frame, including available visits regardless of prespecified time-windows.  
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37 The performance of the final models was found acceptable for DAPSA28 remission and DAPSA28  
38 moderate response but poor for 12-month drug retention. This suggests that additional factors such  
39 as e.g. socio-economic parameters, comorbidities and biomarkers (imaging and serological) are still  
40 needed for better prediction of treatment retention and response.  
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45 In conclusion, baseline predictors of remission, response and drug retention in European patients  
46 with PsA treated with a first TNFi were identified, five of which were common across the  
47 outcomes. The consistency of predictors across registries and treatment outcomes, despite  
48 heterogeneity in patient characteristics and treatment practices, indicate that the baseline predictors  
49 emerging from our pooled analyses may be considered generalisable from the country- to disease-  
50 level.  
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## Acknowledgements

The EuroSpA Research Collaboration Network was financially supported by Novartis Pharma AG. Novartis had no influence on the data collection, statistical analyses, manuscript preparation or decision to submit the manuscript.

**Funding:** This work was supported by Novartis Pharma AG.

**Conflicts of interest:** Louise Linde, Lykke M. Ørnbjerg, Stylianos Georgiadis and Simon H.

**Rasmussen:** research grants from Novartis; **Johan Askling:** PI for agreements between Karolinska Institutet and Abbvie, Astra-Zeneca, BMS, Eli Lilly, Galapagos, Janssen, MSD, Pfizer, Roche, Samsung Bioepis, Sanofi, and UCB; **Brigitte Michelsen:** research grant from Novartis; **Johan K. Wallman:** speaking fee from AbbVie, Amgen. Research support from AbbVie, Amgen, Eli Lilly, Novartis, Pfizer; **Bjorn Gudbjornsson:** consulting and/or Speaking fees from Amgen and Novartis; **Dan C. Nordström:** consulting and/or speaking fees from Abbvie, BMS, Lilly, MSD, Novartis, Pfizer, Roche and UCB; **Jiří Vencovský:** consulting and/or speaking fees from Abbvie, Biogen, Boehringer Ingelheim, Eli Lilly, Gilead, Merck Sharp and Dohme, Pfizer and UCB; **Florenzo Iannone:** consulting and/or speaking from Abbvie, Amgen, AstraZeneca, BMS, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, UCB; **Alberto Cauli:** consulting and/or speaking fees from Abbvie, Amgen, Biogen, BMS, Galapagos, Eli Lilly, Janssen, Novartis, Pfizer, UCB; **Anne Gitte Loft:** Research Grant from Novartis, and speaking and/or consulting fees from AbbVie, Janssen, Lilly, MSD, Novartis, Pfizer, Roche, and UCB; **Bente Glinthorg:** Research grants: Pfizer, Abbvie, BMS; Karin Laas: consulting and/or speaking fees from Amgen, Johnson and Johnson and Novartis; **Ziga Rotar:** speaking or consultancy fees from Abbvie, Novartis, MSD, Medis, Biogen, Eli Lilly, Pfizer, Sanofi, Lek, Janssen; **Matija Tomšič:** consulting and/or speaking fees from Abbvie, Amgen, Biogen, Eli Lilly, Janssen, Medis, MSD, Novartis, Pfizer, Sanofi, Sandoz-Lek; **Gary J. Macfarlane:** research grant from GSK; **Burkhard Möller:** speaking fee from: Eli-Lilly, Janssen, Novartis, Pfizer. Grants from Amgen; **Marleen van de Sande:** research grant and/or consulting fee, and/or speaker fee from Eli Lilly, Novartis, UCB, Janssen, Abbvie; **Catalin Codreanu:** speaking and consultancy fees from AbbVie, Amgen, Boehringer Ingelheim, Ewopharma, Lilly, Novartis, Pfizer; **Michael J. Nissen:** consulting and/or speaking fees from AbbVie, Eli Lilly, Janssens, Novartis and Pfizer; **Sukran Erten:** speaking fees from Celltrion,

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4 Pfizer, MSD, **Maria J. Santos**: speaker fees from Abbvie, AstraZeneca, Lilly, Novartis and Pfizer;  
5  
6 **Elsa Vieira-Sousa**: research grants from MSD, Pfizer, UCB. Speaker fees from Novartis, Abbvie,  
7  
8 MSD, Celgene, UCB; **Merete L. Hetland**: research grants from Abbvie, Biogen, BMS, Celltrion,  
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10 Eli Lilly, Janssen Biologics B.V, Lundbeck Fonden, MSD, Medac, Pfizer, Roche, Samsung  
11  
12 Biopies, Sandoz, Novartis and **Mikkel Østergaard**: research grants from Abbvie, BMS, Merck,  
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14 Celgene and Novartis, and speaker and/or consultancy fees from Abbvie, BMS, Boehringer-  
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16 Ingelheim, Celgene, Eli-Lilly, Hospira, Janssen, Merck, Novartis, Novo, Orion, Pfizer, Regeneron,  
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18 Roche, Sandoz, Sanofi and UCB. The remaining authors have declared no conflicts of interest.  
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21 **Data availability:** The data in this article was collected in the individual registries and made  
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23 available for secondary use through the EuroSpA Research Collaboration Network  
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25 [<https://eurospa.eu/#registries>]. Relevant patient level data may be made available on reasonable  
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27 request to the corresponding author, but will require approval from all contributing registries.  
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4 **Figure 1. Classification of patients starting their first TNF-inhibitor with regards to**  
5 **DAPSA28 remission (A) and DAPSA28 moderate response (B) at six months.**  
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8 \*Excluding Italy and Spain due to no available CRP; \*\*according to the opinion of the clinician;  
9 \*\*\*remission: n=1,723 (panel A)/response: n=1,803 (panel B); \*\*\*\*no remission: n=5,231 (panel  
10 A)/no response: n=3,472 (panel B); \*\*\*\*\*including patients stopping TNFi *after* 6 months for all  
11 reasons, patients stopping TNFi *within* 6 months for other reasons and patients continuing on TNFi  
12 but without an assessment.  
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17 TNFi: Tumor Necrosis Factor alpha inhibitor; DAPSA28: Disease Activity index for PSoriatic  
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Table 1. Baseline characteristics of PsA patients starting a first TNFi, pooled and stratified by registry.

Country	All	Czech Republic	Denmark	Finland	Iceland	Italy	Norway	Portugal	Romania	Slovenia	Spain	Sweden	Switzerland	Turkey
Registry	Pooled	ATTRA	DANBIO	ROB-FIN	ICEBIO	GISEA	NOR-DMARD	Reuma.pt	RRBR	Biorx.si	BIOBADASER	SRQ	SCQM	TURKBIO
Number of patients, n	13369	718	2090	234	306	1591	717	675	86	367	445	5225	628	287
<b>Demography and diagnosis</b>														
Age at treatment start, years	49 (40-58)	49 (40-57)	48 (39-56)	48 (40-56)	50 (39-59)	51 (42-59)	47 (39-57)	49 (40-57)	52 (47-61)	51 (43-57)	50 (40-57)	50 (40-59)	50 (40-58)	41 (34-51)
Age at diagnosis, years	43 (34-52)	40 (31-49)	43 (34-52)	40 (30-48)	43 (32-53)	45 (36-54)	41 (32-51)	42 (33-51)	47 (39-55)	43 (35-51)	45 (36-53)	43 (34-53)	44 (35-54)	36 (29-45)
Time since diagnosis, years	3 (1-8)	6 (2-12)	3 (1-7)	5 (2-11)	4 (1-9)	3 (1-7)	3 (1-9)	4 (2-8)	4 (2-6)	5 (2-10)	3 (1-7)	3 (1-8)	2 (1-6)	3 (1-7)
Men, n (%)	6385 (48%)	386 (54%)	928 (44%)	118 (50%)	126 (41%)	733 (46%)	345 (48%)	338 (50%)	37 (43%)	194 (53%)	227 (51%)	2552 (49%)	293 (47%)	108 (38%)
BMI, kg/m <sup>2</sup>	27.0 (24.1-30.5)	28.1 (24.9-32.0)	27.2 (23.9-30.5)	27.8 (25.2-31.4)	30.1 (26.8-34.4)	26.2 (23.5-29.4)	NA	26.5 (24.0-29.4)	28.5 (25.5-31.8)	26.6 (23.8-29.7)	27.1 (24.2-30.7)	NA	26.5 (23.5-29.8)	28.1 (25.3-31.2)
Current smokers, n (%)	1865 (17%)	89 (16%)	582 (29%)	14 (12%)	26 (15%)	67 (8%)	131 (22%)	74 (16%)	4 (5%)	54 (15%)	98 (23%)	528 (12%)	127 (24%)	71 (26%)
Fulfilling the CASPAR criteria, n (%)	2497 (93%)	675 (95%)	284 (96%)	NA	47 (94%)	71 (96%)	NA	455 (89%)	79 (92%)	364 (99%)	NA	NA	502 (87%)	20 (87%)
<b>Clinical measures</b>														
Swollen joint count (28)	2 (0-5)	7 (3-10)	1 (0-3)	2 (1-5)	4 (2-6)	1 (0-3)	1 (0-3)	3 (1-6)	-	6 (3-9)	2 (1-4)	2 (0-5)	2 (0-4)	2 (0-4)
Swollen joint count (66)	3 (1-7)	9 (5-12)	3 (0-6)	3 (1-6)	-	1 (0-4)	NA	4 (1-8)	-	NA	NA	3 (1-6)	3 (1-6)	-
Tender joint count (28)	4 (1-9)	10 (5-13)	4 (1-8)	3 (1-6)	4 (2-6)	3 (1-8)	2 (1-6)	4 (2-9)	-	8 (4-12)	3 (1-6)	4 (2-8)	3 (1-7)	4 (1-8)
Tender joint count (68)	7 (3-12)	12 (8-19)	8 (4-14)	4 (2-9)	-	4 (2-10)	NA	7 (3-13)	-	NA	NA	6 (3-11)	6 (2-11)	-
CRP, mg/l	6 (3-14)	15 (6-28)	5 (2-12)	6 (3-13)	8 (3-15)	NA	5 (2-11)	8 (4-19)	-	7 (3-16)	NA	5 (2-12)	5 (2-10)	9 (3-17)

ESR, mm/hr	15 (7-29)	30 (17-45)	NA	14 (5-24)	NA	15 (8-30)	12 (6-22)	24 (11-42)	-	24 (12-40)	17 (7-34)	12 (6-24)	11 (6-20)	NA
Physician global score (mm)	40 (25-60)	65 (50-80)	25 (15-40)	38 (26-51)	56 (41-70)	50 (30-70)	30 (21-40)	50 (36-65)	-	60 (40-70)	NA	40 (30-50)	40 (30-60)	31 (20-62)
DAPSA28, units	25 (17-37)	41 (30-52)	23 (16-34)	21 (16-33)	28 (21-34)	NA	17 (12-26)	28 (19-40)	-	38 (26-51)	NA	24 (17-35)	19 (13-29)	26 (17-34)
DAPSA (original), units	25 (18-35)	36 (27-43)	26 (19-36)	21 (15-29)	-	NA	NA	26 (19-37)	-	NA	NA	23 (17-31)	21 (15-32)	-
DAS28-CRP, units	4.2 (3.3-5.0)	5.2 (4.6-5.8)	4.0 (3.1-4.8)	3.9 (3.2-4.7)	4.3 (3.9-4.9)	NA	3.5 (2.7-4.3)	4.3 (3.6-5.2)	-	5.0 (4.1-5.6)	NA	4.1 (3.3-4.8)	3.6 (2.7-4.5)	4.2 (3.2-4.9)
<b>Treatment</b>														
n (%)														
Infliximab	2251 (17%)	99 (14%)	576 (28%)	56 (24%)	188 (61%)	114 (7%)	91 (13%)	52 (8%)	8 (9%)	26 (7%)	39 (9%)	907 (17%)	64 (10%)	31 (11%)
Etanercept	4654 (35%)	126 (18%)	495 (24%)	60 (26%)	67 (22%)	657 (41%)	211 (29%)	270 (40%)	18 (21%)	63 (17%)	170 (38%)	2290 (44%)	147 (23%)	80 (28%)
Adalimumab	3987 (30%)	352 (49%)	626 (30%)	87 (37%)	9 (3%)	614 (39%)	87 (12%)	198 (29%)	41 (48%)	172 (47%)	132 (30%)	1312 (25%)	243 (39%)	114 (40%)
Certolizumab pegol	847 (6%)	47 (7%)	208 (10%)	6 (3%)	0 (0%)	28 (2%)	190 (26%)	12 (2%)	0 (0%)	31 (8%)	38 (9%)	248 (5%)	16 (3%)	23 (8%)
Golimumab	1630 (12%)	94 (13%)	185 (9%)	25 (11%)	42 (14%)	178 (11%)	138 (19%)	143 (21%)	19 (22%)	75 (20%)	66 (15%)	468 (9%)	158 (25%)	39 (14%)
TNFi start year*, n (%)														
2009-2014	7541 (56%)	344 (48%)	1231 (59%)	179 (76%)	144 (47%)	1254 (79%)	469 (65%)	336 (50%)	0 (0%)	219 (60%)	95 (21%)	2708 (52%)	452 (72%)	110 (38%)
2015-2018	5828 (44%)	374 (52%)	859 (41%)	55 (24%)	162 (53%)	337 (21%)	248 (35%)	339 (50%)	86 (100%)	148 (40%)	350 (79%)	2517 (48%)	176 (28%)	177 (62%)
Concomitant csDMARD (%)**	7832 (59%)	588 (82%)	1311 (63%)	190 (81%)	129 (42%)	916 (58%)	529 (74%)	463 (69%)	85 (99%)	285 (78%)	323 (73%)	2539 (49%)	361 (57%)	113 (39%)
<b>Patient reported outcomes (PROs)</b>														



Patient pain score (mm)	61 (42-77)	70 (50-80)	63 (43-78)	54 (36-72)	67 (50-78)	60 (50-80)	48 (29-65)	60 (48-80)	-	70 (56-80)	NA	61 (43-75)	60 (40-70)	75 (55-80)
Patient fatigue score (mm)	65 (41-80)	65 (50-80)	70 (50-84)	NA	70 (50-80)	NA	45 (15-70)	NA	NA	NA	NA	64 (41-78)	-	70 (50-75)
Patient global score (mm)	64 (45-80)	70 (58-80)	72 (52-87)	51 (31-70)	74 (54-85)	60 (50-80)	51 (31-70)	64 (48-80)	-	70 (60-80)	60 (50-80)	60 (42-75)	60 (40-80)	70 (54-75)
HAQ (units)	0.9 (0.5-1.4)	1.2 (0.9-1.6)	1.0 (0.6-1.5)	0.9 (0.5-1.4)	1.2 (0.8-1.5)	1.0 (0.4-1.5)	0.5 (0.2-0.9)	1.1 (0.5-1.5)	-	1.1 (0.5-1.6)	NA	0.9 (0.5-1.2)	0.8 (0.4-1.1)	0.8 (0.6-0.9)
<b>Comorbidities and conditions associated with PsA</b>														
Psoriasis	1904 (83%)	NA	378 (100%)	203 (87%)	NA	NA	NA	311 (61%)	41 (48%)	328 (89%)	-	NA	529 (89%)	90 (100%)
Uveitis	63 (3%)	NA	NA	10 (4%)	NA	NA	NA	1 (0%)	0 (0%)	6 (2%)	14 (3%)	NA	32 (5%)	NA
Inflammatory bowel disease	148 (8%)	NA	-	7 (3%)	NA	92 (100%)	NA	0 (0%)	0 (0%)	2 (1%)	NA	NA	22 (4%)	-
Cardiovascular disease	898 (26%)	262 (36%)	-	67 (29%)	NA	123 (100%)	108 (23%)	9 (2%)	43 (50%)	116 (32%)	18 (5%)	NA	108 (24%)	-
Diabetes	396 (12%)	57 (8%)	-	16 (7%)	NA	119 (100%)	27 (6%)	27 (5%)	14 (16%)	27 (7%)	34 (9%)	NA	27 (6%)	-
Kidney	92 (3%)	7 (1%)	NA	0 (0%)	NA	-	7 (1%)	8 (2%)	7 (8%)	4 (1%)	1 (0%)	NA	9 (3%)	NA
Data are as observed, median (interquartile range) or percentage. Percentages are calculated based on the number of patients with available data, unless stated otherwise. Cells are marked with "-" if based on <50 patients.														
NA: Not available; BMI: Body Mass Index; CASPAR: CIASsification criteria for Psoriatic ARthritis; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; DAPSA28: Disease Activity index for Psoriatic Arthritis in 28 joints; DAPSA (original): based on 66/68 joints; DAS28-CRP: disease activity score in 28 joints based on CRP; HLA-B27: Human Leukocyte Antigen subtypes B*2701-2759; TNFi: Tumor Necrosis Factor Inhibitor; csDMARD: conventional synthetic Disease Modifying Anti-Rheumatic Drug; HAQ: Health Assessment Questionnaire.														
*2009 was chosen as the first three biological Disease Modifying Anti-Rheumatic Drugs (bDMARDs) (adalimumab, etanercept and infliximab) from that year were all well-established treatment options across the European countries. 2015 was chosen as secukinumab was approved as the first non-TNFi bDMARD treatment option that year; **patients with no registration of concomitant use of csDMARDs were considered not using such drugs, all data are thus considered available.														

Table 2. Summary of predictors of DAPSA28 remission after 6 months of treatment with the first TNFi per registry\* for registries with EPV per available independent variables  $\geq 1$ .

Country	Czech Republic	Denmark	Finland	Iceland	Norway	Portugal	Romania	Slovenia	Sweden	Switzerland	Turkey	Row sum**
Registry	ATTRA	DANBIO	ROB-FIN	ICEBIO	NOR-DMARD	Reuma.pt	RRBR	Biorx.si	SRQ	SCQM	TURKBIO	
Patients with DAPSA28 remission assessment, n	480	1496	113	177	546	383	82	287	3074	157	159	
DAPSA28 remission, n (%)	127 (27)	344 (23)	35 (31)	45 (25)	163 (30)	102 (27)	17 (21)	51 (18)	748 (24)	37 (24)	54 (34)	
EPV per available IVs	9.1	24.6	2.7	3.2	12.5	7.8	1.7	3.9	57.5	2.6	3.9	
Age at treatment start, years	-	-	-		-	-		-	-	-	-	9
Men	+	+	+	+	+	+	-		+		+	9
Time since diagnosis, years	+	+			+		+		+			5
BMI, kg/m <sup>2</sup>	-	-			NA	-	-		NA	-		5
Current smokers		-								-		2
Concomitant csDMARD							constant					0
1 <sup>st</sup> TNFi start, year (2015-2018)***		+					constant			+		2
CRP>10 mg/l****	+	+					constant		+			3
Patient pain score, mm		-	-	-	-	-					+	6
Patient fatigue score, mm		-	NA		-	NA	NA	NA	-	-	-	5
Physician global score, mm	-		+						-			3

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HAQ, units	-	-		-				-	-			5
Swollen joint count (28)					+				+			2
<b>Tender joint count (28)</b>		-	-	-	-			-	-	-		7
Sum of independent predictors*****	7	11	5	4	7	4	3	3	9	6	4	
Total number of available IVs*****	14	14	13	14	13	13	10	13	13	14	14	

Baseline variables that are identified as predictors in at least half of registries in which the variable is available are highlighted in bold.

DAPSA28: Disease Activity index for PSoriatic Arthritis in 28 joints; EPV: events-per-variable; IVs: independent variables; BMI: Body Mass Index; ; csDMARD: conventional synthetic Disease Modifying Anti-Rheumatic Drug; CRP: C-reactive protein; HAQ: Health Assessment Questionnaire; TNFi: Tumor Necrosis Factor Inhibitor; +: Odds Ratio (OR)>1; -: OR<1; constant: dichotomous variable, where only one category was available in the registry ; NA: variable not delivered by the registry; \*Italy and Spain excluded due to no available CRP; \*\*number of times a variable is selected as a predictor; \*\*\*TNFi initiation since January 1<sup>st</sup> 2009 was chosen as the start of data collection, as the first three bDMARDs (adalimumab, etanercept and infliximab) were then well-established treatment options across the European countries. 2015 was chosen as the separator between the time periods, as secukinumab was approved as the first non-TNFi bDMARD treatment option that year; \*\*\*\*the CRP cut-off was decided based on the various detection limits used across registries; \*\*\*\*\*sum of predictors selected per cohort; \*\*\*\*\*number of independent variables (after excluding NA and constant variables).

Table 3. Summary of predictors of DAPSA28 moderate response after 6 months of treatment with the first TNFi per registry\* for registries with EPV per available independent variables  $\geq 1$ .

Country	Czech Republic	Denmark	Finland	Iceland	Norway	Portugal	Romania	Slovenia	Sweden	Switzerland	Turkey	Row sum**
Registry	ATTRA	DANBIO	ROB-FIN	ICEBIO	NOR-DMARD	Reuma.pt	RRBR	Biorx.si	SRQ	SCQM	TURKBIO	
Patients with DAPSA28 response assessment, n	462	1172	84	68	472	268	20	275	2205	116	133	
DAPSA28 moderate response, n (%)	265 (57)	317 (27)	34 (41)	13 (19)	143 (30)	106 (40)	11 (55)	124 (45)	711 (32)	17 (15)	62 (47)	
EPV per available IVs	15.5	22.6	2.6	0.9	11	8.2	1	9.5	54.7	1.2	4.4	
Age at treatment start, years	-	-	-		-			-	-			6
Men		+			+	+			+			4
Time since diagnosis, years	+	+	+						+			4
BMI, kg/m <sup>2</sup>	-	-			NA	-		-	NA	-		5
Current smokers		-	-				constant	-	-	-		5
Concomitant csDMARD							constant		+			1
1 <sup>st</sup> TNFi start, year (2015-2018)***	+						constant					1
CRP>10 mg/l****	+	+			+	+	constant	+	+			6
Patient pain score, mm		+				-			+		+	4
Patient fatigue score, mm		-	NA		-	NA	NA	NA	-	-	-	5
Physician global score, mm	-					-		+				3

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HAQ, units	-	-			-			-	-			5
<b>Swollen joint count (28)</b>	<b>+</b>	<b>+</b>			<b>+</b>	<b>+</b>	<b>+</b>		<b>+</b>	<b>+</b>	<b>+</b>	<b>8</b>
Tender joint count (28)		<b>+</b>						<b>+</b>				2
Sum of independent predictors*****	8	11	3	0	6	6	1	7	10	4	3	
Total number of available IVs*****	14	14	13	14	13	13	9	13	13	14	14	

Baseline variables that are selected as predictors in at least half of registries in which the variable is available are highlighted in bold.

DAPSA28: Disease Activity index for Psoriatic Arthritis in 28 joints; EPV: events-per-variable; IVs: independent variables; BMI: Body Mass Index; csDMARD: conventional synthetic Disease Modifying Anti-Rheumatic Drug; CRP: C-reactive protein; HAQ: Health Assessment Questionnaire; TNFi: Tumor Necrosis Factor Inhibitor; +: Odds Ratio (OR)>1; -: OR<1; constant: dichotomous variable, where only one category was available in the registry; NA: variable not delivered by the registry; \*Italy and Spain excluded due to no available CRP; \*\*number of times a variable is selected as a predictor; \*\*\*TNFi initiation since January 1<sup>st</sup> 2009 was chosen as the start of data collection, as the first three bDMARDs (adalimumab, etanercept and infliximab) were then well-established treatment options across the European countries. 2015 was chosen as the separator between the time periods, as secukinumab was approved as the first non-TNFi bDMARD treatment option that year; \*\*\*\*the CRP cut-off was decided based on the various detection limits used across registries; \*\*\*\*\*sum of predictors selected per cohort; \*\*\*\*\*number of independent variables (after excluding NA and constant variables).

Table 4. Summary of predictors of 12-month drug retention on the first TNFi per registry for registries with EPV per available independent variables  $\geq 1$ .

Country	Czech Republic	Denmark	Finland	Iceland	Italy	Norway	Portugal	Romania	Slovenia	Spain	Sweden	Switzerland	Turkey	Row sum*
Registry	ATTRA	DANBIO	ROB-FIN	ICEBIO	GISEA	NOR-DMARD	Reuma.pt	RRBR	Biorx.si	BIOBADASER	SRQ	SCQM	TURKBIO	
Number of patients	718	2090	234	306	1591	717	675	86	367	445	5225	628	287	
12-months drug retention, n (%)	504 (70)	1225 (59)	150 (64)	206 (67)	861 (54)	389 (54)	512 (76)	63 (73)	231 (63)	281 (63)	3468 (66)	387 (62)	184 (64)	
EPV per available IVs	15.3	61.8	6.5	7.1	60.9	25.2	12.5	1.9	10.5	18.2	135.2	17.2	7.4	
Age at treatment start, years					-	-			-	-	-		-	6
Men	+	+	+			+	+		+	+	+	+	+	10
Time since diagnosis, years	+	+		+	-		+		+	+	+	+		9
BMI, kg/m <sup>2</sup>			+		+	NA			-		NA			3
Current smokers				-			-	+			-		-	5
Concomitant csDMARD	+	+	-			+	+			+		+		7
1 <sup>st</sup> TNFi start, year (2015-2018)**	-	-		-	-	-	-	constant	-	-		-	-	10
CRP>10 mg/l***		+			NA	+	+			NA	+		+	5
Patient pain score, mm			-	-		-	-			NA	-			5
Patient fatigue score, mm		-	NA		NA	+	NA	NA	NA	NA	-			3
Physician global score, mm	+									NA				1

HAQ, units										NA				0
Swollen joint count (28)	+				-						+			3
Tender joint count (28)	-	-									-	-	-	5
Sum of independent predictors****	7	7	4	4	5	7	7	1	5	5	9	5	6	
Total number of available IVs*****	14	14	13	14	12	13	13	12	13	9	13	14	14	

Baseline variables that are selected as predictors in at least half of registries in which the variable is available are highlighted in bold.

EPV: events-per-variable; IVs: independent variables; BMI: Body Mass Index; csDMARD: conventional synthetic Disease Modifying Anti-Rheumatic Drug; CRP: C-reactive protein; HAQ: Health Assessment Questionnaire; TNFi: Tumor Necrosis Factor Inhibitor; +: Odds Ratio (OR)>1; -: OR<1; constant: dichotomous variable, where only one category was available in the registry e; NA: variable not delivered by the registry.

\*number of times a variable is selected as a predictor; \*\*TNFi initiation since January 1<sup>st</sup> 2009 was chosen as the start of data collection, as the first three bDMARDs (adalimumab, etanercept and infliximab) were then well-established treatment options across the European countries. 2015 was chosen as the separator between the time periods, as secukinumab was approved as the first non-TNFi bDMARD treatment option that year; \*\*\*the CRP cut-off was decided based on the various detection limits used across registries; \*\*\*\*sum of predictors selected per cohort; \*\*\*\*\*number of independent variables (after excluding NA and constant variables).

Table 5. Univariate and final multivariate analyses for predicting DAPSA28 remission and DAPSA28 moderate response at 6 months and 12-month drug retention on the first TNFi in pooled data (derivation cohorts) for registries with EPV  $\geq 1$ .

	Prediction of DAPSA28 remission (n=3435)				Prediction of DAPSA28 moderate response (n=2537)				Prediction of 12-month drug retention (n=6642)			
	Univariate		Multivariate		Univariate		Multivariate		Univariate		Multivariate	
Patients achieving the outcome, n (%)	836 (24%)				860 (34%)				4170 (63%)			
	OR (95% CI)				OR (95% CI)				OR (95% CI)			
Age at treatment start, years	0.97	(0.97 - 0.98)	0.97	(0.96 - 0.98)	0.98	(0.97 - 0.99)			0.99	(0.99 - 1.00)	0.99	(0.99 - 1.00)
Men	2.43	(2.07 - 2.86)	1.85	(1.54 - 2.23)	1.96	(1.66 - 2.31)	1.71	(1.42 - 2.06)	1.66	(1.50 - 1.84)	1.47	(1.32 - 1.63)
Time since diagnosis, years	1.01	(1.00 - 1.02)			1.02	(1.01 - 1.04)	1.03	(1.01 - 1.04)	1.02	(1.01 - 1.03)		
BMI, kg/m <sup>2</sup>	0.97	(0.94 - 0.99)	0.98	(0.95 - 1.00)	0.97	(0.95 - 0.99)	0.97	(0.95 - 0.99)	1.00	(0.98 - 1.01)		
Current smokers	0.69	(0.54 - 0.87)	0.74	(0.57 - 0.96)	0.82	(0.65 - 1.04)			0.73	(0.63 - 0.84)	0.77	(0.66 - 0.89)
Concomitant csDMARD	1.15	(0.98 - 1.35)			1.40	(1.17 - 1.68)	1.23	(1.01 - 1.50)	1.11	(1.00 - 1.22)		
1 <sup>st</sup> TNFi start, year (2015-2018)*	1.19	(1.01 - 1.39)			1.21	(1.02 - 1.42)			0.73	(0.66 - 0.81)	0.65	(0.58 - 0.72)
CRP>10 mg/l**	1.32	(1.09 - 1.58)	1.52	(1.22 - 1.89)	1.93	(1.62 - 2.29)	1.61	(1.33 - 1.95)	1.22	(1.07 - 1.39)	1.24	(1.08 - 1.43)
Patient pain score, mm	0.98	(0.97 - 0.98)			0.99	(0.99 - 1.00)	1.01	(1.00 - 1.01)	0.99	(0.99 - 0.99)	0.99	(0.99 - 1.00)



<b>Patient fatigue score, mm</b>	0.98	(0.97 - 0.98)	0.99	(0.98 - 0.99)	0.99	(0.98 - 0.99)	0.99	(0.98 - 0.99)	0.99	(0.99 - 0.99)	1.00	(0.99 - 1.00)
Physician global score, mm	0.99	(0.98 - 0.99)	0.99	(0.98 - 1.00)	1.01	(1.00 - 1.01)			1.00	(1.00 - 1.00)		
HAQ, units	0.32	(0.27 - 0.38)	0.57	(0.45 - 0.71)	0.73	(0.63 - 0.84)	0.75	(0.61 - 0.91)	0.79	(0.72 - 0.87)		
Swollen joint count (28)	0.97	(0.94 - 0.99)	1.05	(1.01 - 1.08)	1.08	(1.06 - 1.10)			1.00	(0.98 - 1.01)		
Tender joint count (28)	0.92	(0.90 - 0.93)			1.02	(1.00 - 1.03)			0.97	(0.96 - 0.98)	0.97	(0.96 - 0.99)
<b>Age at treatment start, years (41-49)***</b>							0.72	(0.56 - 0.92)				
<b>Age at treatment start, years (50-57)</b>							0.46	(0.36 - 0.60)				
<b>Age at treatment start, years (58-84)</b>							0.48	(0.37 - 0.63)				
<b>Time since diagnosis, years (2<sup>nd</sup> quartile)***</b>			1.20	(0.89 - 1.60)							1.12	(0.95 - 1.31)
<b>Time since diagnosis, years (3<sup>rd</sup> quartile)</b>			1.42	(1.09 - 1.84)							1.29	(1.11 - 1.50)
<b>Time since diagnosis, years (4<sup>th</sup> quartile)</b>			1.66	(1.26 - 2.20)							1.43	(1.21 - 1.69)
Patient pain score, mm (44-61)			0.64	(0.49 - 0.83)								
Patient pain score, mm (62-75)			0.77	(0.58 - 1.04)								
Patient pain score, mm (76-100)			0.80	(0.55 - 1.16)								
Swollen joint count (2-4)***							1.73	(1.38 - 2.16)				

Swollen joint count (5-28)							2.22	(1.74 - 2.84)				
Tender joint count (3-4)***			0.87	(0.66 - 1.15)								
Tender joint count (5-8)			0.60	(0.45 - 0.80)								
Tender joint count (9-28)			0.52	(0.36 - 0.74)								
AUROC (95% CI) ****			0.75 (0.73 - 0.77)				0.73 (0.70 - 0.75)				0.64 (0.62 - 0.65)	

Baseline variables that are common predictors across all outcomes are highlighted in bold. Registries with EPV  $\geq 1$  in derivation cohort, considering all independent variables, were included in all models (RRBR excluded from all analyses, ICEBIO and SCQM excluded from DAPSA28 response analyses).

DAPSA28: Disease Activity index for Psoriatic Arthritis in 28 joints; TNFi: Tumor Necrosis Factor Inhibitor; OR: odds ratio; 95CI: 95% confidence interval. BMI: Body Mass Index; csDMARD: conventional synthetic Disease Modifying Anti-Rheumatic Drug; CRP: C-reactive protein; HAQ: Health Assessment Questionnaire; AUROC: Area under the Receiver Operating Curve.

\*TNFi initiation since January 1<sup>st</sup> 2009 was chosen as the start of data collection, as the first three bDMARDs (adalimumab, etanercept and infliximab) were then well-established treatment options across the European countries. 2015 was chosen as the separator between the time periods, as secukinumab was approved as the first non-TNFi bDMARD treatment option that year; \*\*the CRP cut-off was decided based on the various detection limits used across registries; \*\*\*continuous independent variables were categorized if linearity assumption was violated. Cut-offs for time since diagnosis in DAPSA28 remission: 2<sup>nd</sup> quartile (2-3 yrs), 3<sup>rd</sup> quartile (4-9 yrs) and 4<sup>th</sup> quartile (10-56 yrs); 12-month drug retention: 2<sup>nd</sup> quartile (2 -3 yrs), 3<sup>rd</sup> quartile (4-8 yrs) and 4<sup>th</sup> quartile (9-56 yrs); \*\*\*\*AUROC was calculated in derivation cohort.

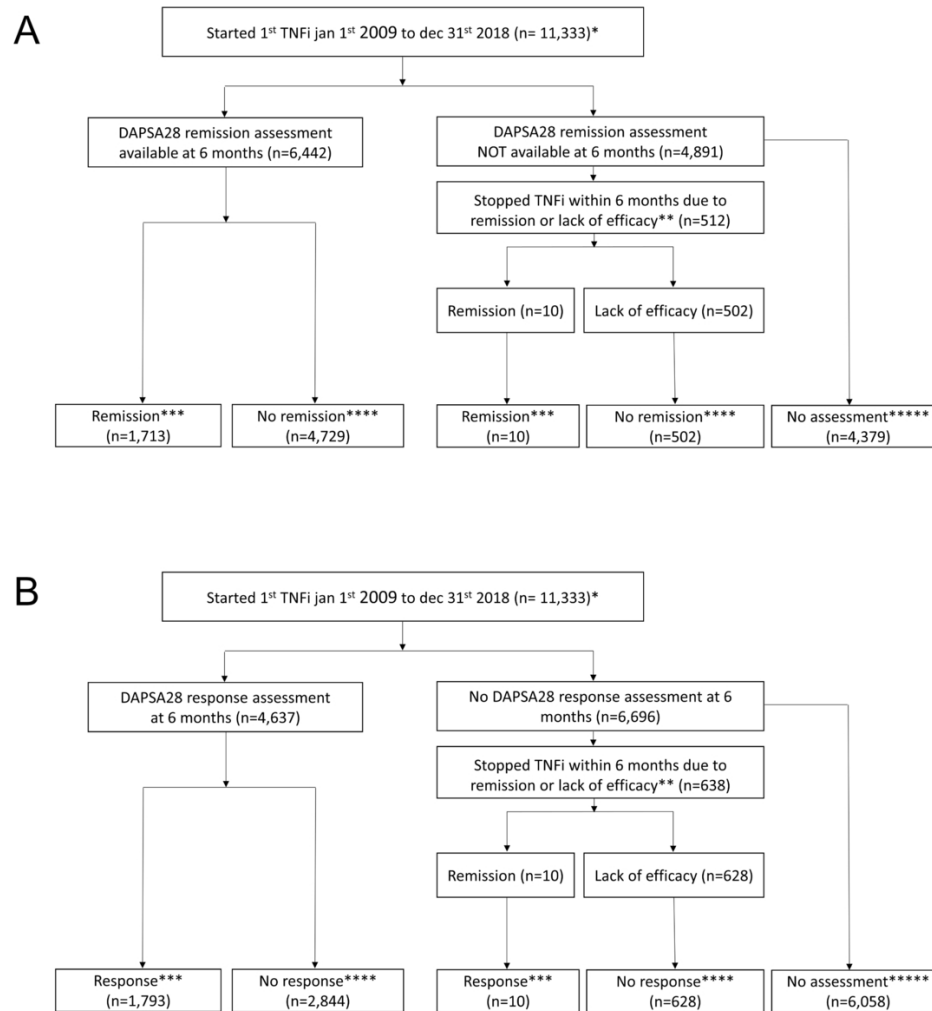


Figure 1

97x107mm (300 x 300 DPI)