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Comparing DAPSA, DAPSA28, and DAS28-CRP in Patients With Psoriatic Arthritis Initiating a First Tumor Necrosis Factor Inhibitor Across Nine European Countries

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Objective. Because 66/68 joint counts are not always performed in routine care, we aimed to determine which of the modified 28-joint disease activity index for psoriatic arthritis (DAPSA28) or 28-joint disease activity score with C-reactive protein (DAS28-CRP) should be preferred for monitoring disease activity in psoriatic arthritis (PsA) when the original DAPSA (66/68 joints) is not available.

Methods. Prospectively collected real-world data of European bionaive patients with PsA initiating a first tumor necrosis factor inhibitor were pooled. Remission and response status were evaluated at 6 months by remission (DAPSA ≤ 4, DAPSA28 ≤ 4, and DAS28-CRP < 2.6), response (75% improvement for DAPSA and DAPSA28), and combined EULAR good/moderate responses for DAS28-CRP. Logistic regression analyses on multiple imputed data were used to identify baseline predictors.

Results. Remission and response cohorts included 3,159 and 1,866 patients, respectively. The 6-month proportions achieving remission/response were DAPSA (27%/44%), DAPSA28 (28%/44%), and DAS28-CRP (59%/80%). Of 14 possible baseline predictors, 11 predicted both DAPSA and DAPSA28 remission (8 of which also predicted their response, indicated by "*"): longer disease duration*, male sex*, and higher CRP* were positive, whereas older age*, higher body mass index*, patient fatigue*, and global, physician global, health assessment questionnaire score*, and tender and swollen* joint counts were negative predictors. Eight and five of these predicted DAS28-CRP remission and response, respectively.

Conclusion. In patients with PsA, DAPSA28 should be preferred over DAS28-CRP as a substitute for DAPSA when 66/68 joint counts are not available because of the large overlap in remission and response status and in predictors between DAPSA and DAPSA28.

INTRODUCTION

The disease activity index for psoriatic arthritis (DAPSA) includes 66/68 joint counts, C-reactive protein (CRP), and patient pain and global assessments.[1] The DAPSA does not directly address other psoriatic arthritis (PsA) manifestations (eg, enthesitis, dactylitis, skin and nail involvement, or axial disease). The 66/68 joint count is approved by the Group for Research and Assessment of Psoriasis and PsA and the Outcome Measures in Rheumatology group to monitor disease activity in patients with

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SIGNIFICANCE & INNOVATIONS

- Patients with psoriatic arthritis (PsA) may experience the involvement of distal interphalangeal joints or feet; therefore, the disease activity index for PsA (DAPSA), which includes 66/68 joints, is considered a gold standard outcome measure in monitoring disease activity in PsA.
- In routine care, 66/68 swollen and tender joint counts are not always performed, and this study investigates which of the 28 joint count–based outcome measures, DAPSA based on 28 joint counts (DAPSA28) or disease activity score with 28 joint counts and C-reactive protein (DAS28-CRP), is the most suitable when 66/68 joint counts are not available.
- We conclude that DAPSA28 should be preferred over DAS28-CRP when 66/68 joint counts are not available because of the large overlap in remission and response status and in predictors between DAPSA and DAPSA28.

PsA.[2] In routine clinical practice, however, 66/68 swollen and tender joint counts are not always performed, and therefore a simplified version of DAPSA based on 28 joint counts (DAPSA28) has been developed and validated in patients with PsA.[3] In addition, although originally developed for rheumatoid arthritis, the disease activity score with 28 joint counts, a patient global assessment, and CRP (DAS28-CRP) or erythrocyte sedimentation rate has been used as an outcome measure in randomized controlled trials of PsA.[4,5] Outcome measures based on 28 joint counts, however, do not capture the joint involvement in patients with phenotypic PsA (eg, with arthritis in distal interphalangeal joints or feet) and may therefore be less suitable than DAPSA.[6,7]

Clinical remission and response rates according to DAPSA28 and DAS28-CRP have been reported alongside DAPSA in observational studies of treatment effectiveness in PsA.[8–13] It remains unclear, however, which of those two outcome measures renders results that are the most congruent with DAPSA and which should thus be preferred in settings in which only 28 joint counts are available. We aimed to investigate whether DAPSA28 or DAS28-CRP is the most suitable in this respect by exploring the remission and response status of individual patients and the baseline predictors thereof according to DAPSA, DAPSA28, and DAS28-CRP in European bionaive patients who initiated a first tumor necrosis factor inhibitor (TNFi) in routine care.

PATIENTS AND METHODS

Data sources. This study included secondary use of anonymized, prospectively collected data from nine European registries with available DAPSA, DAPSA28, and DAS28-CRP scores: ATTRA (Czech Republic), DANBIO (Denmark), ROB-FIN (Finland), ICEBIO (Iceland), Reuma.pt (Portugal), RRBR (Romania), SRQ (Sweden), SCQM (Switzerland), and TURKBIO (Turkey). The registries are further described in Linde et al.[14] Data were uploaded by individual registries onto a secure central server.

Patients and visits. Patients were included in the study if they had a registered clinical diagnosis of PsA, were aged ≥18 years at diagnosis, and had initiated a first TNFi treatment between January 1, 2009, and December 31, 2018. Data from the following time points were considered: baseline visit (30 days before to 30 days after the registered date of TNFi treatment start) and 6 months' follow-up (90 to 270 days after the treatment start date).

Cohorts and baseline demographics. To cover both the remission and response outcomes (see the "Outcomes" section), we defined two cohorts as follows. One cohort covered the remission outcomes and required complete data on DAPSA, DAPSA28, and DAS28-CRP at the 6-month follow-up visit (hereafter called the "remission cohort"). Another cohort covered the response outcomes and included patients who had complete data on DAPSA, DAPSA28, and DAS28-CRP at *both* the baseline and 6-month follow-up visits (hereafter called the "response cohort").

Demography (age, disease duration, sex, body mass index [BMI], and smoking status), treatment (TNFi and concomitant conventional synthetic disease-modifying antirheumatic drugs [csDMARDs]), patient-reported outcomes (pain, fatigue, and global scores [all on a 0–100 scale] and health assessment questionnaire [HAQ]), and clinical measures (28 and 66/68 swollen and tender joint counts, CRP, and physician global score [0–100 scale]) were recorded at baseline.

Outcomes. The outcomes of interest were 6-month clinical remission and response according to DAPSA, DAPSA28, and

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DAS28-CRP, respectively. Clinical remission was defined as ≤4 for both DAPSA and DAPSA28[1,3] and as <2.6 for DAS28-CRP.[5] For both DAPSA and DAPSA28, a clinical response was defined as a 75% improvement between baseline and 6 months' follow-up (ie, a moderate response using the definition for DAPSA) because no validated definition is available for DAPSA28 response.[1,3] For DAS28-CRP, the EULAR good and moderate responses were merged into a combined category.[15]

Ethics. All participating registries had obtained the necessary approvals from the relevant local authorities before transferring their data for this study. Thus, because the study uses secondary, anonymized data, no separate ethics approval is necessary.

Statistics. Data from the individual registries were pooled. The distribution of missing components in DAPSA, DAPSA28, and DAS28-CRP at baseline and 6 months follow-up was described. Descriptive analyses of the baseline patient characteristics were performed in patients included in the remission and response cohorts.

Remission and response. The proportions of patients achieving the remission and response outcomes in the corresponding cohorts were calculated. Venn diagrams were used to describe overlaps in individual patients achieving the outcomes. Baseline characteristics according to any DAPSA remission and response versus only DAS28-CRP remission and response at 6 months were described. Additionally, DAPSA, DAPSA28, and DAS28-CRP remission and responses were stratified according to the baseline 66 swollen joint count in the response cohort (0–1, 2–4, and ≥5 swollen joints).

Prediction analyses. In the remission and response cohorts, respectively, logistic regression analyses were used to identify baseline predictors of the outcomes of interest. The following 14 baseline patient characteristics were included as potential predictors: sex, smoking status (current vs past/never smokers), CRP (≤10 mg/L vs >10 mg/L), and csDMARD use (yes vs no) as categorical variables and age, disease duration, BMI, patient pain, fatigue and global visual analog scores, HAQ, physician global score, and swollen and tender joint counts as continuous variables. The baseline 66/68 joint counts were included as potential predictors when assessing the DAPSA outcomes, whereas the 28 joint counts were instead included when assessing the DAPSA28 and DAS28-CRP outcomes. Finally, the gross domestic product per capita was forced into the multivariable models to adjust for heterogeneity across the registries.[16] Multiple imputation by chained equations was used to impute missing baseline patient characteristics (20 imputed datasets). For each remission and response outcome, the selection of potential predictors was performed separately in each of the 20 imputed datasets. Initially, univariable logistic regression analyses were performed for all potential predictors. Variables with a *P* value <0.20 in univariable analyses were included in the initial multivariable model, where a backward stepwise selection was applied. Next, potential predictors excluded in univariable analyses were introduced one at a time in the multivariable model, and their significance was tested. The final model included the predictors that appeared in at least half of the 20 separate models. Once the set of predictors was selected, the model was fitted to all 20 imputed datasets and the model estimates were pooled according to Rubin's rules.[17] Likelihood ratio tests were used to assess all models. Internal validation combining multiple imputation and bootstrapping was applied to assess the performance of the final multivariable models.[18] The area under the receiver operating curve was assessed for performance by calculating the bootstrap 0.632 plus the estimate to account for potential overfitting in the internal validation process.

RESULTS

Of 10,256 patients with PsA initiating a first TNFi between January 1, 2009, and December 31, 2018, baseline visits were missing for 2,278 patients (22%) and 6 months' follow-up visits for 3,241 patients (32%) (Supplementary Table 1). The highest proportion of missing components was seen for the 66/68 joint counts (Supplementary Table 2).

Remission and response. The remission and response cohorts comprised 3,159 and 1,866 patients, respectively, with similar baseline patient characteristics (Table 1). Patients excluded from the cohorts received concomitant csDMARDs more often and had a higher physician global score compared with those included in the cohorts, but otherwise the baseline characteristics were similar (Supplementary Tables 3 and 4).

In the remission cohort, the proportions of patients in DAPSA, DAPSA28, and DAS28-CRP remission at 6 months were 861 (27%), 896 (28%), and 1,866 (59%), respectively, whereas 822 (26%) achieved clinical remission by all three definitions. Six patients achieved DAPSA remission only, and none achieved DAPSA28 remission only; 937 patients (30%) achieved DAS28-CRP remission only (Figure 1A). The patients in DAS28-CRP remission (but not in DAPSA/DAPSA28 remission) were more often women and had higher baseline patient pain, fatigue, and global scores compared with those in DAPSA/DAPSA28 remission combined (Supplementary Table 5). Remission rates when stratifying patients on baseline 66 swollen joint count (0–1, 2–4, and ≥5, respectively) were similar (Supplementary Table 6).

In the response cohort, the proportions of patients who had achieved DAPSA and DAPSA28 moderate response were 817 (44%) and 820 (44%), whereas 1,493 (80%) had achieved a EULAR good/moderate response, and 743 (40%) had

Table 1. Baseline characteristics of patients with PsA in the remission and response cohorts*

	Remission cohort[a] (n = 3,159)		Response cohort[b] (n = 1,866)	
	Available data, n (%)	Median (IQR) or n (%)	Available data, n (%)	Median (IQR) or n (%)
Demographics				
Age at treatment start, years	3,159 (100)	49 (40–58)	1,866 (100)	49 (40–58)
Time since diagnosis, years	2,548 (81)	4 (1–9)	1,575 (84)	4 (1–10)
Men	3,159 (100)	1,599 (51%)	1,866 (100)	968 (52)
BMI, kg/m^2	986 (31)	27.7 (24.6–31.3)	701 (38)	27.7 (24.5–31.5)
Current smokers	2,872 (91)	407 (14)	1,691 (91)	250 (15)
Treatment				
TNFi	3,159 (100)	–	1,866 (100)	–
Infliximab	–	533 (17)	–	291 (16)
Etanercept	–	1,093 (35)	–	630 (34)
Adalimumab	–	900 (28)	–	548 (29)
Certolizumab pegol	–	195 (6)	–	125 (7)
Golimumab	–	438 (14)	–	272 (15)
TNFi start year	3,159 (100)	–	1,866 (100)	–
2009–2014	–	1,394 (44)	–	819 (44)
2015–2018	–	1,765 (56)	–	1,047 (56)
Concomitant csDMARD	3,159 (100)	2,009 (64)	1,866 (100)	1,313 (70)
Patient-reported outcomes				
Patient pain score (0–100 mm)	2,407 (76)	64 (44–75)	1,866 (100)	65 (45–77)
Patient fatigue score (0–100 mm)	1,341 (42)	66 (44–80)	968 (52)	66 (42–80)
Patient global score (0–100 mm)	2,445 (77)	64 (46–79)	1,866 (100)	64 (46–80)
HAQ (0–3)	2,292 (73)	1.0 (0.5–1.4)	1,755 (94)	1.0 (0.6–1.4)
Clinical measures				
28 swollen joint count (0–28)	2,442 (77)	3 (1–6)	1,866 (100)	3 (1–6)
66 swollen joint count (0–66)	2,069 (65)	4 (2–8)	1,866 (100)	4 (2–8)
28 tender joint count (0–28)	2,440 (77)	4 (2–9)	1,866 (100)	5 (2–9)
68 tender joint count (0–68)	2,082 (66)	8 (4–13)	1,866 (100)	8 (4–14)
CRP, mg/L	2,450 (78)	7 (3–17)	1,866 (100)	8 (3–18)
Physician global score (0–100 mm)	1,392 (44)	50 (30–65)	1,118 (60)	50 (30–68)
Composite scores				
DAPSA, units	1,900 (60)	26 (19–37)	1,866 (100)	26 (19–37)
DAPSA28, units	2,241 (71)	26 (18–39)	1,866 (100)	26 (18–39)
DAS28-CRP, units	2,274 (72)	4.2 (3.4–5.0)	1,866 (100)	4.3 (3.5–5.1)

* Percentages are calculated based on the number of patients with available data. BMI, body mass index; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAPSA28, disease activity index for psoriatic arthritis based on 28 joints; DAS28-CRP, disease activity score in 28 joints based on C-reactive protein; HAQ, Health Assessment Questionnaire; IQR, interquartile range; PsA, psoriatic arthritis; TNFi, tumor necrosis factor inhibitor.
[a] Patients with complete data on DAPSA, DAPSA28, and DAS28-CRP at 6 months.
[b] Patients with complete data on DAPSA, DAPSA28, and DAS28-CRP at baseline and 6 months.

achieved clinical response by all three definitions. Seven patients achieved DAPSA moderate response only, one patient achieved DAPSA28 moderate response only, and 633 (34%) patients achieved EULAR good/moderate response only (Figure 1B). The patients with EULAR good/moderate response only were more often women and had higher baseline patient pain, fatigue, and global scores compared with those with DAPSA/DAPSA28 response combined (Supplementary Table 7). All response rates in the three groups, stratified on baseline 66 swollen joint count, increased by the increasing number of swollen joints at baseline (Supplementary Table 6).

Prediction analyses. All missing values in baseline characteristics (ie, potential predictors) were imputed by multiple imputation by chained equations. In the remission cohort, the range of imputed data was 9% (current smokers) to 69% (BMI), and in the response cohort 6% (HAQ) to 62% (BMI) (Table 1).

In the multivariable logistic regression analyses of DAPSA, DAPSA28, and DAS28-CRP remission, 11, 11, and 9 of the 14 assessed baseline predictors were selected in the remission cohort, respectively (Table 2). The same 11 baseline predictors were selected for DAPSA and DAPSA28, and 8 predictors were common for all three outcomes: longer disease duration, male sex, and higher CRP level were positive predictors, whereas older age, higher BMI, higher patient fatigue and HAQ scores, and more tender joints were negative predictors of remission (Table 2).

In the multivariable logistic regression analyses of DAPSA, DAPSA28, and DAS28-CRP response, 8, 8, and 8 of the 14 assessed baseline predictors were selected, respectively (Table 3). The same eight baseline predictors were selected for DAPSA and DAPSA28, and five predictors were common for all

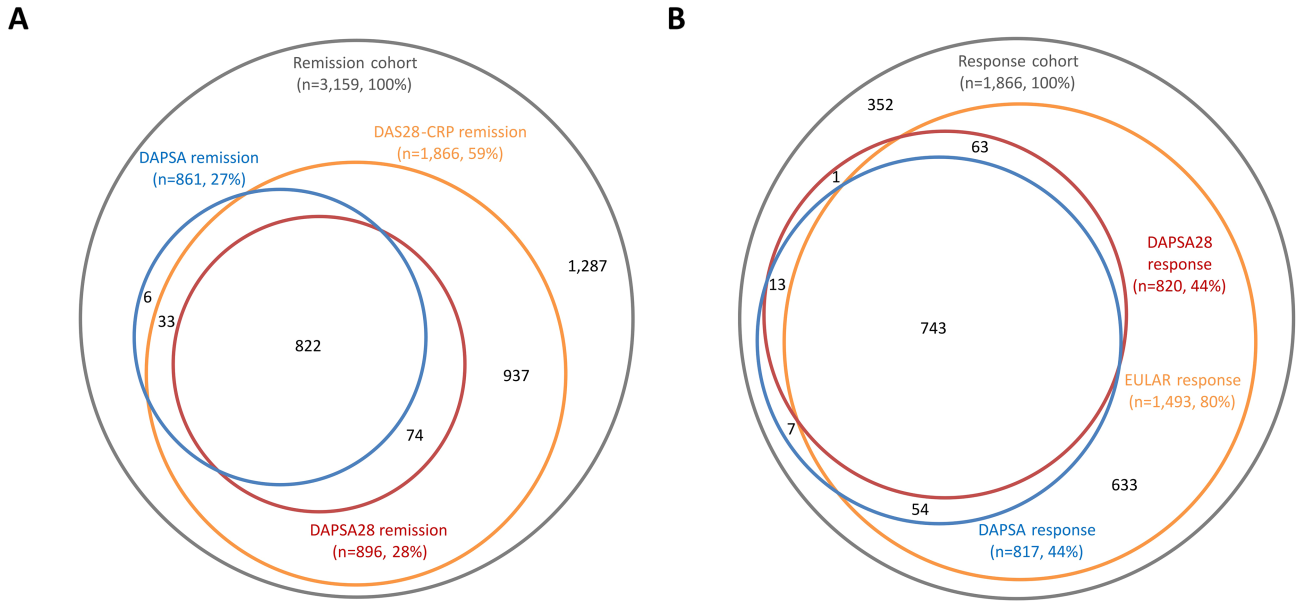

Figure 1. Venn diagrams illustrating remission and response rates and overlaps between the various outcomes in the (A) remission (n = 3,159) and (B) response (n = 1,866) cohorts. The gray circle represents all patients, the blue circle represents patients with DAPSA remission or moderate response, the orange circle represents patients with DAS28-CRP remission or EULAR good/moderate response, and the red circle represents patients with DAPSA28 remission or moderate response. DAPSA28, 28-joint disease activity index for psoriatic arthritis; DAS28-CRP, 28-joint disease activity score with C-reactive protein.

three outcomes: male sex, higher CRP, and more swollen joints were positive predictors, whereas higher BMI and HAQ scores were negative predictors (Table 3). The area under the receiver operating curve (95% confidence interval) ranged from 0.72 (0.69–0.74) (DAPSA28 moderate response) to 0.77 (0.74–0.79) (DAS28-CRP EULAR good/moderate response) (Table 3).

Table 2. Univariable and final multivariable analyses for predicting DAPSA, DAPSA28, and DAS28-CRP remission at 6 months (n = 3,159)*

	DAPSA remission, OR (95% CI)		DAPSA28 remission, OR (95% CI)		DAS28-CRP remission, OR (95% CI)	
	Univariable	Multivariable	Univariable	Multivariable	Univariable	Multivariable
Patients achieving the outcome, n (%)	861 (27)		896 (28)		1,866 (59)	
Age at treatment start,[a] years	0.98 (0.97–0.98)	0.98 (0.97–0.99)	0.98 (0.97–0.98)	0.98 (0.97–0.99)	0.97 (0.97–0.98)	0.98 (0.98–0.99)
Time since diagnosis,[a] years	1.01 (1.00–1.02)	1.02 (1.01–1.04)	1.01 (1.00–1.02)	1.03 (1.01–1.04)	1.00 (0.99–1.01)	1.01 (1.00–1.03)
Men[a]	2.27 (1.93–2.67)	1.74 (1.45–2.10)	2.21 (1.89–2.60)	1.71 (1.42–2.05)	2.34 (2.02–2.70)	1.79 (1.52–2.10)
BMI,[a] kg/m^2	0.95 (0.91–0.99)	0.96 (0.93–1.00)	0.95 (0.91–0.99)	0.96 (0.93–1.00)	0.96 (0.93–0.98)	0.98 (0.95–1.00)
Current smokers	0.72 (0.56–0.91)	–	0.70 (0.54–0.89)	–	0.71 (0.58–0.88)	0.81 (0.64–1.02)
Concomitant csDMARD	1.01 (0.86–1.19)	–	1.01 (0.86–1.18)	–	0.96 (0.83–1.12)	–
CRP >10 mg/L[a,b]	1.33 (1.12–1.59)	1.57 (1.26–1.95)	1.26 (1.06–1.49)	1.49 (1.20–1.85)	1.06 (0.91–1.25)	1.24 (1.02–1.50)
Patient pain score, mm	0.98 (0.97–0.98)	–	0.98 (0.98–0.98)	–	0.98 (0.98–0.98)	–
Patient fatigue score,[a] mm	0.97 (0.97–0.98)	0.99 (0.98–0.99)	0.98 (0.97–0.98)	0.99 (0.98–0.99)	0.98 (0.98–0.98)	0.99 (0.99–1.00)
Patient global score, mm	0.97 (0.97–0.98)	0.99 (0.99–1.00)	0.98 (0.97–0.98)	0.99 (0.99–1.00)	0.98 (0.98–0.98)	–
Physician global score, mm	0.98 (0.98–0.99)	0.99 (0.99–1.00)	0.98 (0.98–0.99)	0.99 (0.99–1.00)	0.99 (0.98–0.99)	–
HAQ,[a] units	0.36 (0.30–0.43)	0.64 (0.50–0.82)	0.36 (0.30–0.44)	0.67 (0.53–0.86)	0.34 (0.29–0.40)	0.52 (0.43–0.64)
Swollen joint count (28)	–	–	0.97 (0.95–0.99)	1.05 (1.01–1.08)	0.93 (0.91–0.94)	–
Tender joint count (28)[a]	–	–	0.93 (0.91–0.95)	0.95 (0.92–0.98)	0.91 (0.89–0.92)	0.93 (0.91–0.94)
Swollen joint count (66)	0.98 (0.96–1.00)	1.03 (1.00–1.06)	–	–	–	–
Tender joint count (68)[a]	0.95 (0.94–0.97)	0.97 (0.96–0.99)	–	–	–	–
AUROC (95% CI)	–	0.74 (0.72–0.76)	–	0.74 (0.71–0.76)	–	0.74 (0.72–0.76)

* The gross domestic product per capita was forced in the multivariable models to adjust for heterogeneity across the registries.[16]
AUROC, area under the receiver operating curve; BMI, body mass index; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAPSA28, disease activity index for psoriatic arthritis based on 28 joints; DAS28-CRP, disease activity score in 28 joints based on C-reactive protein; HAQ, Health Assessment Questionnaire; OR, odds ratio.
[a] Baseline variables that are common predictors across all outcomes.
[b] The CRP cut-off was decided based on the various detection limits used across registries.

Table 3. Univariable and final multivariable analyses for predicting DAPSA and DAPSA28 moderate responses and EULAR response (good/moderate combined) at 6 months (n = 1,866)*

	DAPSA moderate response, OR (95% CI)		DAPSA28 moderate response, OR (95% CI)		EULAR response, OR (95% CI)	
	Univariable	Multivariable	Univariable	Multivariable	Univariable	Multivariable
Patients achieving the outcome, n (%)	817 (44)		820 (44)		1,493 (80)	
Age at treatment start, years	0.98 (0.98–0.99)	0.98 (0.97–0.99)	0.98 (0.98–0.99)	0.98 (0.97–0.99)	1.00 (0.99–1.01)	–
Time since diagnosis, years	1.02 (1.01–1.03)	1.02 (1.01–1.04)	1.02 (1.01–1.04)	1.02 (1.01–1.04)	1.02 (1.00–1.03)	–
Men[a]	2.39 (1.98–2.89)	2.04 (1.66–2.51)	2.07 (1.72–2.50)	1.74 (1.42–2.13)	1.70 (1.36–2.15)	1.69 (1.31–2.19)
BMI,[a] kg/m^2	0.97 (0.94–0.99)	0.97 (0.93–1.01)	0.96 (0.93–0.99)	0.96 (0.92–1.00)	0.98 (0.94–1.02)	0.98 (0.93–1.03)
Current smokers	0.74 (0.56–0.98)	–	0.73 (0.55–0.96)	–	0.99 (0.71–1.39)	–
Concomitant csDMARD	1.32 (1.08–1.61)	–	1.26 (1.03–1.54)	–	1.50 (1.18–1.91)	–
CRP >10 mg/L[a,b]	1.99 (1.65–2.41)	1.54 (1.24–1.91)	1.88 (1.56–2.27)	1.48 (1.20–1.83)	3.58 (2.73–4.73)	2.46 (1.83–3.34)
Patient pain score, mm	0.99 (0.99–1.00)	–	0.99 (0.99–1.00)	–	1.01 (1.00–1.01)	–
Patient fatigue score, mm	0.99 (0.98–0.99)	0.99 (0.98–0.99)	0.99 (0.98–0.99)	0.99 (0.98–0.99)	1.00 (1.00–1.01)	–
Patient global score, mm	0.99 (0.99–0.99)	–	0.99 (0.99–0.99)	–	1.01 (1.01–1.02)	1.01 (1.00–1.02)
Physician global score, mm	1.01 (1.00–1.01)	–	1.00 (1.00–1.01)	–	1.02 (1.02–1.03)	1.01 (1.00–1.02)
HAQ,[a] units	0.78 (0.67–0.91)	0.83 (0.66–1.05)	0.78 (0.66–0.91)	0.80 (0.64–1.00)	1.37 (1.13–1.67)	0.77 (0.59–1.01)
Swollen joint count (28)[a]	–	–	1.11 (1.08–1.14)	1.12 (1.09–1.15)	1.27 (1.21–1.33)	1.18 (1.12–1.24)
Tender joint count (28)	–	–	1.03 (1.02–1.05)	–	1.12 (1.09–1.15)	1.05 (1.02–1.08)
Swollen joint count (66)[a]	1.09 (1.07–1.11)	1.09 (1.07–1.11)	–	–	–	–
Tender joint count (68)	1.02 (1.01–1.03)	–	–	–	–	–
AUROC (95% CI)	–	0.73 (0.70–0.75)	–	0.72 (0.69–0.74)	–	0.77 (0.74–0.79)

* The gross domestic product per capita was forced in the multivariable models to adjust for heterogeneity across the registries.[16]
AUROC, area under the receiver operating curve; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAPSA28, disease activity index for psoriatic arthritis based on 28 joints; HAQ, Health Assessment Questionnaire; OR, odds ratio.
[a] Baseline variables that are common predictors across all outcomes.
[b] The CRP cut-off was decided based on the various detection limits used across registries.

DISCUSSION

In this study, we explored remission and response status and predictors thereof according to DAPSA, DAPSA28, and DAS28-CRP in patients with PsA initiating a first TNFi. We found a large overlap in patients achieving remission or response according to DAPSA and DAPSA28, whereas the overlap between DAPSA and DAS28-CRP was much smaller. Moreover, similar baseline characteristics predicted the DAPSA and DAPSA28 outcomes, whereas the DAS28-CRP outcomes had fewer predictors in common with DAPSA.

DAPSA and DAPSA28 scores performed similarly in the initial validation study cohort,[3] but, to our knowledge, these outcomes have not been reported concurrently in later studies. Few observational studies have reported concurrent DAPSA28 and DAS28 remission rates, and, similar to our findings, the DAPSA28 was the more strict remission criterion.[11,12] In a study of 14,261 patients with PsA from 12 European registries, the 6-month rates for DAPSA28 and DAS28-CRP remission, following the initiation of a first TNFi, were 27% and 56%, respectively.[12] Our study included 9 of these 12 registries and found comparable remission rates (29% and 60%, respectively). A small observational study of 120 patients with PsA receiving TNFi treatment reported 6-month DAPSA28 and DAS28 remission rates of 11% and 72%, respectively. However, the study population differed from ours regarding demographic characteristics (more women with longer disease duration) and disease status (higher disease activity and HAQ scores).[11]

We found a large overlap of patients achieving remission and response according to DAPSA[1] and DAPSA28[3] and similar baseline predictors of both outcomes, suggesting that they capture comparable aspects of PsA, despite the different number of joints included. The proportion of patients achieving the DAS28-CRP[5] outcomes and the baseline predictors thereof differed markedly from those of DAPSA/DAPSA28. Our findings thus support the use of DAPSA28 over DAS28-CRP in PsA when 66/68 joint counts are not available. This is highly relevant because the current study also documented substantial missingness of 66/68 joint counts in the real-life setting across Europe. When available, however, DAPSA would still be preferable because of the characteristic PsA joint involvement that is better captured in a 66/68 joint count. Baseline predictors of remission and response according to DAPSA28 have previously been reported in a comparable cohort, and the identified predictors were similar overall to our current findings.[19] DAPSA and DAS28-CRP were, however, not investigated in the prior study.[19] A few smaller studies have investigated predictors of clinical response during treatment with TNFi in PsA using other response definitions, such as modified-minimal disease activity,[20] ≥50% improvement in American College of Rheumatology response criteria, and a good EULAR response.[21] In these studies, lower baseline DAPSA and higher CRP were predictors of modified-minimal disease activity at 6 months,[20] whereas male sex, polyarthritis, higher CRP and patient

pain assessment, and lower HAQ at baseline predicted American College of Rheumatology response criteria and/or EULAR responses at 12 weeks.[21]

The limitations of this study include a risk for selection bias based on data availability. A minority of all patients had complete data for all three outcome measures, and these patients may not be representative of all patients with PsA initiating a TNFi. However, baseline characteristics of the included versus excluded patients did not reveal major differences. The level of missing data and the variation of missingness across variables are additional limitations. By applying multiple imputation, missing data were addressed in the best possible way, although the potential shortcomings of this approach should be kept in mind (eg, certain variables may not be missing at random in specific registries).

In conclusion, at the group level, DAPSA28 seems to be highly analogous to the gold standard outcome measure DAPSA, notably more so than DAS28-CRP. Our findings thus support the use of DAPSA28 over DAS28-CRP when 66/68 joint counts are not available, which was often the case in this real-life setting from nine European registries.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr Linde had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Linde, Georgiadis, Ørnbjerg.

Acquisition of data. Linde, Georgiadis, Ørnbjerg, Rasmussen, Michelsen, Askling, Di Giuseppe, Wallman, Závada, Pavelka, Bernardes, Matos, Glintborg, Loft, Nordström, Kuusalo, Möller, Nissen, Codreanu, Mogosan, Gudbjornsson, Love, Akleylek, Iannone, Kvien, Rotar, Castrejon, Macfarlane, Hetland, Østergaard.

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ROLE OF THE STUDY SPONSOR

Novartis Pharma AG and IQVIA had no role in the study design or in the collection, analysis, or interpretation of the data, the writing of the manuscript, or the decision to submit the manuscript for publication. Publication of this article was not contingent upon approval by Novartis Pharma AG and IQVIA.

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