## BMJ Open Minimal disease activity and remission in patients with psoriatic arthritis with elevated body mass index: an observational cohort study in the Swiss **Clinical Quality Management cohort**

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#### **ABSTRACT**

**Objective** To assess the impact of elevated body mass index (BMI) in the achievement of minimal disease activity (MDA) and several definitions of remission in patients with psoriatic arthritis (PsA) in Switzerland. Secondarily, to assess the overlapping across the study outcomes.

**Methods** This observational cohort study in the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry included patients with PsA starting their first biologic or targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD) from 1997 to 30 June 2018. Exposure was BMI category at b/tsDMARD start: overweight, obese, and normal weight (reference), Logistic regression was used to assess the achievement of MDA and remission at ≤12 months, as well as treatment persistence at 1 year, in overweight patients and patients with obesity compared with the normal weight group. Remission was defined by Disease Activity for Psoriatic Arthritis (DAPSA), clinical DAPSA (cDAPSA) and 28-joint Disease Activity Score (DAS28). Additionally, overlapping across study outcomes was investigated.

Results The study included 306 (39.5%) normal weight patients, 285 (36.8%) overweight patients and 183 (23.6%) patients with obesity. Compared with the normal weight group, patients with obesity had lower odds of achieving MDA at ≤12 months (adjusted OR (ORadj) 0.45, 95% CI 0.24 to 0.82). This was consistent with the observed reduced odds of achieving DAPSA-remission (ORadj 0.42, 95% CI 0.21 to 0.85), cDAPSA-remission (ORadj 0.51, 95% CI 0.27 to 0.96) and DAS28-remission (ORadj 0.51, 95% CI 0.32 to 0.81) in patients with obesity versus normal weight patients. Among the 125 patients achieving MDA, the majority (81.8% normal weight, 80.0% overweight, 78.9% obese) achieved cDAPSA-remission. No differences were observed in the odds to achieving treatment persistence between the BMI strata.

**Conclusions** Obesity halved the likelihood of achieving MDA and remission in patients with PsA with b/tsDMARDs compared with those with normal weight, while it did not impact treatment persistence. High overlapping of patients achieving the outcomes MDA and cDAPSA-remission was observed across every BMI group.

#### STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ The Swiss Clinical Quality Management in Rheumatic Diseases is a nationwide rheumatology registry that represents one of the largest cohorts of patients with rheumatic diseases, including psoriatic arthritis.
- ⇒ The availability of comprehensive patient information—including data on patient characteristics, clinical features and medication-captured the study exposure, outcome and relevant confounders.
- ⇒ Multiple outcomes of clinical success could be evaluated, including minimal disease activity and remission according to Disease Activity for Psoriatic Arthritis (DAPSA), clinical DAPSA and 28-joint Disease Activity Score, thereby increasing the robustness of our results.
- ⇒ Due to the observational nature of the data, missingness was an intrinsic limitation, however, we used multiple imputation to complete baseline variables relevant for the statistical analyses.
- ⇒ The effect on unidimensional outcomes (eg, dactylitis, axial involvement) was not investigated due to the limited number of patients, however, this remains of interest for future studies.

#### **INTRODUCTION**

Psoriatic arthritis (PsA) is an immunemediated rheumatic disease,1 with an estimated prevalence of 0.05%-0.42%, 2-4 and 5%–41% among patients with psoriasis.<sup>3</sup> PsA is a complex and multifactorial disease,<sup>5</sup> for which pathological features include musculoskeletal involvement, such as inflammation of the peripheral joints (arthritis), the entheses (enthesitis), the axial skeleton (spondylitis) and the finger and toe digits (dactylitis), as well as extra-articular manifestations involving skin and nails, and potentially other organs.<sup>6</sup> Pharmacological treatments include conventional synthetic





disease-modifying antirheumatic drugs (csDMARDs) and biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs).<sup>3</sup> Treatment of PsA aims to maximise health-related quality of life (QoL), through targeting symptoms and structural damage,<sup>7</sup> and it is recommended to target low disease activity, minimal disease activity (MDA) or remission.<sup>6</sup>

One of the most common comorbidities in patients with PsA is obesity, <sup>18</sup> and higher prevalence of obesity has been reported among patients with PsA (23%–37%) compared with the general population. <sup>9-12</sup> Among patients with PsA, obesity has been associated to lower probability of achieving MDA compared with patients with normal weight. <sup>10</sup> <sup>13</sup> <sup>14</sup> Similarly, patients with obesity who have PsA treated with tumour necrosis factor alfa inhibitors (TNFi) showed higher risk of treatment discontinuation compared with patients without obesity, <sup>15</sup> as well as lower odds of achieving treatment response compared with patients without obesity <sup>15</sup> or normal weight patients. <sup>16</sup>

The rationale behind the association between obesity and PsA has been previously discussed.<sup>5</sup> <sup>17</sup> <sup>18</sup> In short, obesity has been described as a low-grade inflammatory disease, <sup>18</sup> and both obesity and PsA share pathological inflammatory pathways. <sup>5</sup> <sup>18</sup> Further evidence supporting the association between obesity and a worse PsA clinical outcome is the association of weight loss with higher rate of achieving MDA. <sup>20</sup> Additionally, obesity is a well-known contributor to the metabolic syndrome (MetS), and MetS was similarly associated with lower likelihood of achieving MDA in patients with PsA. <sup>21</sup>

Despite the growing evidence on the association between obesity and worse clinical response in patients with PsA, most published observational cohort studies on this topic had relatively small sample size. For example, a systematic review investigating the association between obesity and response in immune-mediated inflammatory diseases identified one randomised clinical trial and eight observational cohort studies in patients with PsA, but six of the included observational cohorts had a sample size ≤330. <sup>16</sup>Thus, further investigating this effect, especially in a different and bigger population cohort, remains of interest. Additionally, it is unclear whether the findings would remain consistent across outcome definitions.

Thus, we seek to contribute to the growing body of evidence by performing an observational cohort study aiming to assess the impact of body mass index (BMI) in the achievement of MDA and remission in patients with PsA. Additionally, by including several outcome definitions we aim to investigate the consistency of the findings when considering different aspects of the disease.

#### **METHODS**

#### Study design and data source

We performed an observational cohort study in the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry from 1 January 1997 to 31 July 2019. The SCQM is a national longitudinal population-based cohort

of rheumatic diseases in Switzerland, initiated in 1997.<sup>22</sup> SCQM data are recorded during routine clinical practice, and include information on demographics, body height and weight, life-style habits, antirheumatic medication (with start and stop dates), clinical end points, patient-reported outcomes and health standardised surveys.<sup>12 22</sup> Diagnosis of PsA is recorded in SCQM following the physician's criteria.

#### **Study population**

Patients with PsA (≥18 years old) starting their first b/tsDMARD in the SCQM registry between 1 June 2020 and 30 June 2018 (inclusive) were included in the study. The first recorded start of b/tsDMARD in the SCQM was defined as the index date. Patients with a b/tsDMARD start date before their first registered visit at SCQM were excluded. Similarly, patients without a baseline record on height and weight were excluded.

#### **Exposure**

The exposure of interest was BMI category at the start of the patients' first b/tsDMARD. Baseline BMI (kg/m²) was calculated using height and weight records (online supplemental equation 1) at index date or as close as possible to this date within a 6-month look-back window. Measures of height and weight are taken in the clinic, during routine visits to the rheumatologist. Patients were classified based on BMI as normal weight (BMI <25 kg/m²), overweight (BMI 25.0–29.9 kg/m²) and obese (BMI  $\geq$ 30 kg/m²). The normal weight group was the reference category.

#### **Outcomes**

The primary outcome was defined as achievement of MDA within the first year after the index date. MDA was achieved if at least five of the following seven criteria were met: number of tender joint counts (TJC)  $\leq$ 1; number of swollen joint counts (SJC)  $\leq$ 1; skin manifestation none or almost none; patient's joint pain by visual analogue scale (VAS, 0–100)  $\leq$ 15; patient's assessment on PsA activity by VAS  $\leq$ 20; Health Assessment Questionnaire (HAQ)  $\leq$ 0.5; enthesis points  $\leq$ 1.<sup>23</sup>

Secondary outcomes assessed within the first year were: achievement of Disease Activity for Psoriatic Arthritis (DAPSA) remission, defined as DAPSA ≤4; DAPSA-remission or low disease activity (DAPSA-remLDA), defined as DAPSA ≤14; clinical DAPSA (cDAPSA) remission, defined as cDAPSA ≤4 and 28-joint Disease Activity Score (DAS28) remission, defined as DAS28 <2.6. DAPSA, cDAPSA and DAS28 formulas are described in the online supplemental equations 2–5. DAS28-remission was calculated using erythrocyte sedimentation rate (ESR; DAS28-ESR), however, in cases where follow-up data on DAS28-ESR was missing, DAS28 with C reactive protein (CRP; DAS28-CRP) was used instead, if available.

As a tertiary outcome, persistence with the first b/tsDMARD at the end of month 12 was assessed. We allowed for a permissible gap of 1 month between



treatment courses of the same b/tsDMARD, as illustrated in the online supplemental figure S1.

Patients with missing information on the study outcomes during the follow-up were categorised as not having achieved the corresponding outcome. In a sensitivity analysis, we re-ran our analyses excluding patients with missing information on outcome during follow-up.

#### Follow-up

For primary and secondary outcomes, patients were followed from index date until achievement of outcome or a maximum follow-up of 12 months. For the tertiary outcome (treatment persistence), patients were followed until the earliest of the following: treatment stop, start of a new b/tsDMARD or end of observation period (12 months).

In a secondary analysis, all outcomes were assessed with a maximum follow-up of 9 months and 15 months. This was done to investigate if the findings would differ across shorter and longer follow-up times.

#### **Covariates**

Baseline variables included demographics, BMI, high education, ever smoking, antirheumatic medication (ie, b/tsDMARD, csDMARD, corticosteroid), inflammatory markers or acute phase reactants (ie, ESR, CRP), physician's assessment on disease activity and skin, patientreported disease activity and pain, tender and swollen joint counts (counting 28 joints), composite disease activity scores (ie, DAPSA, cDAPSA, DAS28-ESR), diseasespecific manifestations (ie, musculoskeletal manifestations, dactylitis, enthesitis, sacroilitis, spinal involvement, coxitis, peripheral arthritis, nail manifestation), health standardised surveys (ie, HAQ, Short Form-12 (SF-12)) and comorbidities (ie, cardiovascular event/disease, diabetes or other metabolic problems, depression/ anxiety). Baseline variables were collected at index date, or as close as possible to that date within a 6-month lookback window, except for composite disease activity scores, disease-specific manifestations and health standardised surveys, which were collected with a 3-month look-back window; information on smoking, cardiovascular event/ disease and diabetes, which was included if ever reported prior or at index date and antirheumatic medication, which was collected on the index date.

Additional information on covariates is included in online supplemental text S1.

#### **Data analysis**

Patient baseline characteristics were described, and the overweight and obese categories were compared with the normal weight group (reference group) using  $\chi^2$  test for categorical variables and t-test, analysis of variance or Kruskal-Wallis test for continuous variables. For these tests, missing values did not function as a grouping variable. Statistical significance was defined as p $\leq$ 0.05.

Subsequently, missingness for key baseline variables was addressed with multiple imputation by chained equation (MICE) using the *mice* package<sup>24</sup> in the R Statistical Software.<sup>25</sup> MICE was performed for each study outcome separately, using 50 imputations with 15 interactions for each set. Variables included in the imputations, their original missingness and corresponding applied imputation models are presented in the online supplemental table S1. The 48.32% of the study population had complete information on every variable included in the MICE for the main analysis (online supplemental figure S2). Convergence of imputations was assessed by visual inspection of density plots (online supplemental figure S3).

To investigate the association between BMI categories and the study outcomes, multivariable logistic regression models were conducted (outcome specific) for individual imputed datasets, and the results were pooled to a single estimate according to Rubin's rules. These models were conducted first, including only sex and age as covariates, and second, adding clinical confounders (full-adjusted). Confounders were chosen based on clinical rational and direct acyclic graphs (online supplemental figure S4), and included: sex (male; female), age, high education (yes/no), ever smoking (yes/no), b/tsDMARD (TNFi; other biologic; tsDMARD), csDMARD at index date (yes/ no) and corticosteroid use at index date (yes/no). Additionally, sensitivity analyses were performed whereby we added the respective composite disease activity score or health standardised survey to the fully adjusted models for primary and secondary outcomes to assess their potential mediating impact on the analyses. Another sensitivity analysis addressed the 1-year outcomes after excluding patients with underweight (BMI  $<18.5 \,\mathrm{kg/m^2}$ )

Lastly, to compare the overlapping across study outcomes, the proportion of patients achieving each outcome (per BMI group) was summarised, and the overlapping of patients achieving individual primary and secondary outcomes during the first year was illustrated with a Venn diagram.

#### **Patient and public involvement**

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

#### **RESULTS**

The study included 774 adult patients with PsA starting their first b/tsDMARD. Online supplemental figure S5 illustrates the cohort selection process. Among included patients, 306 (39.53%) were normal weight, 285 (36.82%) were overweight and 183 (23.64%) were obese. Baseline patient characteristics (prior to imputation) are presented in table 1. Compared with the normal weight group, overweight patients had higher SJC, were less frequently women and had older mean age. Both overweight patients and patients with obesity had lower frequency of high education, and higher patient-reported disease activity and joint pain, while only patients with obesity had higher CRP levels. Compared with the normal

**Table 1** Patient characteristics at start of first biologic or targeted synthetic disease-modifying antirheumatic drug (b/tsDMARD), prior imputation, stratified by body mass index (BMI)

	Normal weight (n=306)	Overweight (n=285)	P value	Obese (n=183)	P value
Sex, women	172 (56.21)	126 (44.21)	0.01	101 (55.19)	0.90
Age, years (mean (SD))	47.59 (13.20)	50.60 (12.52)	0.01	49.50 (11.03)	0.10
High education (high technical school or university)	80 (26.14)	42 (14.74)	0.00	27 (14.75)	0.01
Missing	54 (17.65)	51 (17.89)		41 (22.4)	
Smoker (ever smoker)	77 (25.16)	84 (29.47)	0.28	54 (29.51)	0.35
Disease duration, years (mean (SD))	5.85 (8.07)	5.54 (6.98)	0.63	4.51 (6.02)	0.06
Missing	6 (1.96)	6 (2.11)		5 (2.73)	
b/tsDMRAD			0.87		0.35
TNFi biologic*	279 (91.18)	262 (91.93)		160 (87.43)	
Other biologic	9 (2.94)	9 (3.16)		6 (3.28)	
tsDMARD‡	18 (5.88)	14 (4.91)		17 (9.29)	
csDMARD at index	152 (49.67)	151 (52.98)	0.47	100 (54.64)	0.33
Corticosteroid (prednisone) at index	38 (12.42)	38 (13.33)	0.83	17 (9.29)	0.36
HLA-B27+	39 (12.75)	28 (9.82)	0.30	20 (10.93)	0.88
Missing	141 (46.08)	132 (46.32)		92 (50.27)	
ESR (mm/hour) (median (IQR))	10.00 (5.00, 22.00)	12.00 (6.00, 22.00)	0.15	15.00 (6.00, 23.00)	0.10
Missing	38 (12.42)	43 (15.09)		24 (13.11)	
CRP (mg/dL) (median (IQR))	0.52 (0.20, 0.90)	0.60 (0.30, 1.10)	0.18	0.80 (0.40, 1.20)	0.03
Missing	48 (15.69)	52 (18.25)		27 (14.75)	
Swollen joint counts (0-66) (mean (SD))	4.70 (5.31)	5.78 (7.17)	0.05	4.88 (5.34)	0.73
Missing	36 (11.76)	18 (6.32)		18 (9.84)	
Tender joint counts (0-68) (mean (SD))	8.20 (9.23)	9.18 (10.36)	0.25	8.72 (9.80)	0.58
Missing	36 (11.76)	18 (6.32)		19 (10.38)	
Physician global disease activity (1–10) (mean (SD))	4.42 (2.04)	4.58 (1.88)	0.32	4.41 (1.85)	0.96
Missing	16 (5.23)	9 (3.16)		6 (3.28)	
Physician global skin manifestation			0.11		0.07
None	75 (24.51)	48 (16.84)		31 (16.94)	
Almost none	55 (17.97)	55 (19.3)		34 (18.58)	
Mild	56 (18.3)	66 (23.16)		36 (19.67)	
Mild to moderate	35 (11.44)	30 (10.53)		18 (9.84)	
Moderate	27 (8.82)	35 (12.28)		33 (18.03)	
Moderate to severe	19 (6.21)	28 (9.82)		13 (7.10)	
Severe	9 (2.94)	6 (2.11)		4 (2.19)	
Missing	30 (9.80)	17 (5.96)		14 (7.65)	
Patient's assessment on PsA activity (1–10) (mean (SD))	5.08 (2.73)	5.57 (2.50)	0.05	6.05 (2.56)	0.00
Missing	82 (26.80)	57 (20.00)		46 (25.14)	
Patient's joint pain (1-10) (mean (SD))	4.88 (2.65)	5.48 (2.39)	0.01	6.18 (2.36)	<0.001
Missing	76 (24.84)	54 (18.95)		44 (24.04)	
Musculoskeletal manifestations	232 (75.82)	213 (74.74)	0.84	140 (76.50)	0.95
Dactylitis	101 (33.01)	106 (37.19)	0.33	66 (36.07)	0.55
Enthesitis	116 (37.91)	103 (36.14)	0.72	67 (36.61)	0.85
Sacroilitis	72 (23.53)	64 (22.46)	0.83	27 (14.75)	0.03

Continued

0.01

0.00

0.01

0.05

0.69



Table 1

Continued

SF-12 pcs (mean (SD))

Cardiovascular event/disease

Diabetes or other metabolic problems

Missina

Missing

HAQ (mean (SD))

Depression/Anxiety

Normal weight (n=306) Overweight (n=285) P value Obese (n=183) P value Spinal involvement 81 (26.47) 70 (24.56) 0.66 40 (21.86) 0.30 Coxitis 13 (4.25) 8 (2.81) 0.47 15 (8.20) 0.11 Peripheral arthritis 141 (46.08) 94 (51.37) 138 (48.42) 0.63 0.30 Nail manifestation 64 (20.92) 62 (21.75) 0.88 47 (25.68) 0.27 DAPSA (mean (SD)) 23.14 (15.73) 27.94 (18.23) 26.56 (14.18) 0.01 0.07 118 (38.56) 103 (36.14) 77 (42.08) Missing cDAPSA (mean (SD)) 22.04 (15.21) 26.39 (17.57) 0.01 25.60 (13.70) 0.04 Missing 107 (34.97) 80 (28.07) 71 (38.80) DAS28-ESR (mean (SD)) 3.34 (1.26) 3.61 (1.33) 0.02 3.44 (1.22) 0.43 34 (18.58) Missing 51 (16.67) 49 (17.19) SF-12 mcs (mean (SD)) 45.87 (11.36) 45.11 (11.66) 0.49 43.85 (11.68) 0.11 Missing 77 (25.16) 78 (27.37) 51 (27.87)

37.63 (9.71)

78 (27.37)

0.79 (0.58)

59 (20.70)

39 (13.68)

20 (7.02)

17 (5.96)

38.95 (10.67)

77 (25.16)

0.71 (0.66)

60 (19.61)

26 (8.50)

10 (3.27)

13 (4.25)

Values are the number and column percentage, unless otherwise specified. Significance tests compare overweight or obese categories with the normal weight group (reference) using  $\chi^2$  test for categorical variables, and t-test or analysis of variance for continuous variables, but Kruskal-Wallis test for ESR and CRP. For these tests, missing values did not function as a grouping variable. Normal weight (BMI <25 kg/m²); overweight (BMI 25.0–29.9 kg/m²); obese (BMI  $\geq$ 30 kg/m²).

CRP, C reactive protein; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DAPSA, Disease Activity Index for Psoriatic Arthritis; DAS28, 28-joint Disease Activity Score; ESR, erythrocyte sedimentation rate; HAQ, Health Assessment Questionnaire; HLA-B27+, human leucocyte antigen B27 positive; mcs, mental component summary; n, sample size; pcs, physical component summary; PsA, psoriasis arthritis; SF-12, Short-Form 12 health survey; TNFi, tumor necrosis factor alpha inhibitor.

weight category, DAPSA and DAS28 were elevated in the overweight group, while cDAPSA was higher in both overweight and obese BMI categories. HAQ and SF-12 with physical components were worse in the patients with obesity, and patients with obesity were more likely to have had a cardiovascular event/disease than the normal weight group.

Results from the logistic regression for the primary analysis are presented in figure 1. Compared with the normal weight group, patients with obesity had significantly lower odds of achieving MDA within the first year, with an adjusted OR (ORadj) of 0.45 (95% CI 0.24 to 0.82). Similarly, both overweight patients and patients with obesity had >50% reduced odds of achieving DAPSA-remission (overweight ORadj 0.44 (95% CI 0.24 to 0.79) and obese ORadj 0.42 (95% CI 0.21 to 0.85)), compared with normal weight patients. Additionally, patients with obesity had reduced odds of achieving cDAPSA-remission (ORadj 0.51 (95% CI 0.27 to 0.96)) and DAS28-remission (ORadj 0.51 (95% CI 0.32 to 0.81)) within the first year.

No differences were observed across BMI categories on achievement of DAPSA-remLDA or treatment persistence at the end of month 12.

0.18

0.20

0.06

0.06

0.45

35.79 (9.04)

51 (27.87)

0.93 (0.61)

48 (26.23)

31 (16.94)

14 (7.65)

10 (5.46)

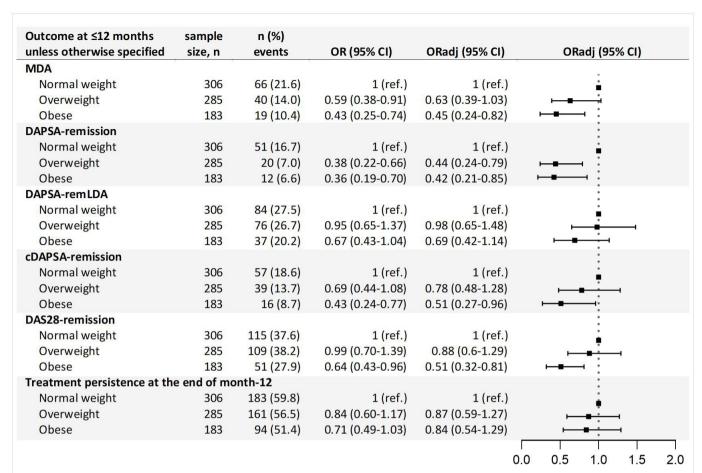
The secondary analyses showed that extending the maximum follow-up to 15 months resulted in similar findings to those from the 12 months analyses (table 2). However, in the 9-month analyses, the associations of obesity with DAPSA-remission and with cDAPSA-remission were no longer significant (table 2).

In the sensitivity analysis in which the respective composite disease activity score or health standardised survey was included in the model, the previously observed findings in the high BMI groups were attenuated, with the exception of obesity and achievement of MDA (online supplemental table S2). The sensitivity analysis excluding patients with missing information on outcome during the 1-year follow-up yielded stronger reduced odds of achieving MDA and remission among abnormal BMI categories versus the normal weight group (online supplemental table S3). The sensitivity analysis excluding

<sup>\*</sup>Adalimumab, etanercept, infliximab, certolizumab, golimumab.

<sup>†</sup>Abatacept, secukinumab, tocilizumab, ustekinumab.

<sup>±</sup>Apremilast.



**Figure 1** Results from the multivariable logistic regression investigating the association between body mass index categories and various clinical outcomes. Maximum follow-up 12 months.

cDAPSA-remission, clinical Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSA-remission, Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSA-remission; DAPSA-remission or low disease activity; DAS28-remission, 28-joint Disease Activity Score remission; MDA, Minimal Disease Activity; n, number; OR, odds ratio adjusting for: sex, age; ORadj, odds ratio adjusting for: sex, age, high educational level, smoker, biologic or targeted synthetic disease-modifying antirheumatic drugs, conventional synthetic disease-modifying antirheumatic drugs, corticosteroid; ref., reference.

the 12 patients with BMI  $<18.5 \text{ kg/m}^2$  yielded similar results to the main study findings (online supplemental table S4).

The frequency of achieved outcomes (with 12 months follow-up) per BMI category are presented in figure 2. Overall, 125 patients achieved MDA, 83 DAPSA-remission, 197 DAPSA-remLDA, 112 cDAPSA-remission and 275 DAS28-remission within the first year. Across all outcomes, patients with obesity had a lower prevalence of achieved outcomes. DAS28-remission and treatment persistence had the highest prevalence in all groups, with 37.58% and 59.80% achieved among normal weight patients and 27.87% and 51.37% among patients with obesity, respectively.

The overlap of patients achieving the outcomes during the first year is illustrated in figure 3, complemented with numerical values in online supplemental table S5. Among the 125 patients achieving MDA (66 normal weight, 40 overweight, 19 with obesity), 80 also achieved DAPSA-remission, of which 48 (72.73%) were normal weight, 20 (50.00%) were overweight and 12 (63.16%) were with obesity. Similarly, among patient with MDA, 54 (81.82%) normal weight, 32 (80.00%) overweight and 15 (78.95%) patients with obesity also achieved cDAPSA-remission. Additionally, MDA overlapped with every remission outcome in 45 (68.18%) normal weight, 18 (45.00%) overweight and 11 (57.89%) patients with obesity.

#### DISCUSSION

This observational cohort study found that patients with obesity had a significant 49%–58% reduced odds of achieving MDA, DAPSA-remission, cDAPSA-remission and DAS28-remission within the first year, when compared with normal weight patients. Conversely, being overweight was only associated with a reduced odds of achieving DAPSA remission. In both high BMI categories, the

Result from the multivariable logistic regression investigating the association between body mass index (BMI) categories and various clinical outcomes, with maximum follow-up 9 months and 15 months Table 2

		_	Maximim follow-iin 9months	Omonthe		Maximim follow-iin 15 months	15 months
	sample size, n	n (%) events	OR (95% CI)	ORadj (95% CI)	N events	OR (95% CI)	ORadj (95% CI)
MDA							
Normal weight	306	45 (14.7)	1 (ref.)	1 (ref.)	86 (28.1)	1 (ref.)	1 (ref.)
Overweight	285	21 (7.4)	0.47 (0.27–0.82)	0.52 (0.28-0.96)	61 (21.4)	0.67 (0.45–0.98)	0.75 (0.48–1.15)
Obese	183	12 (6.6)	0.41 (0.21–0.80)	0.44 (0.21–0.94)	30 (16.4)	0.50 (0.31–0.80)	0.57 (0.34-0.96)
DAPSA-remission							
Normal weight	306	31 (10.1)	1 (ref.)	1 (ref.)	67 (21.9)	1 (ref.)	1 (ref.)
Overweight	285	11 (3.9)	0.35 (0.17-0.72)	0.40 (0.18–0.88)	31 (10.9)	0.42 (0.26–0.68)	0.50 (0.30-0.84)
Obese	183	8 (4.4)	0.41 (0.18–0.92)	0.49 (0.20–1.18)	17 (9.3)	0.37 (0.21–0.67)	0.47 (0.25–0.87)
DAPSA-remLDA							
Normal weight	306	47 (15.4)	1 (ref.)	1 (ref.)	117 (38.2)	1 (ref.)	1 (ref.)
Overweight	285	37 (13.0)	0.81 (0.51–1.30)	0.88 (0.52-1.50)	104 (36.5)	0.91 (0.65–1.27)	0.90 (0.62-1.31)
Obese	183	22 (12.0)	0.75 (0.43–1.29)	0.75 (0.40–1.40)	52 (28.4)	0.64 (0.43-0.95)	0.66 (0.42–1.03)
cDAPSA-remission							
Normal weight	306	36 (11.8)	1 (ref.)	1 (ref.)	77 (25.2)	1 (ref.)	1 (ref.)
Overweight	285	22 (7.7)	0.62 (0.35–1.09)	0.70 (0.38-1.30)	53 (18.6)	0.65 (0.43-0.98)	0.75 (0.48–1.16)
Opese	183	12 (6.6)	0.53 (0.27-1.06)	0.64 (0.31–1.35)	23 (12.6)	0.43 (0.26-0.72)	0.55 (0.32-0.95)
DAS28-remission							
Normal weight	306	68 (22.2)	1 (ref.)	1 (ref.)	153 (50)	1 (ref.)	1 (ref.)
Overweight	285	64 (22.5)	1.01 (0.68–1.49)	0.91 (0.58–1.43)	140 (49.1)	0.91 (0.65–1.28)	0.89 (0.61–1.3)
Opese	183	29 (15.8)	0.67 (0.41–1.08)	0.50 (0.28-0.89)	70 (38.3)	0.62 (0.42–0.91)	0.57 (0.36-0.88)
Treatment persistence at the end of follow-up	e at the end of follow	dn-					
Normal weight	306	204 (66.7)	1 (ref.)	1 (ref.)	159 (52)	1 (ref.)	1 (ref.)
Overweight	285	184 (64.6)	0.86 (0.60–1.21)	0.91 (0.60–1.36)	148 (51.9)	0.96 (0.69–1.34)	0.97 (0.67–1.42)
Obese	183	111 (60.7)	0.77 (0.52–1.12)	0.91 (0.57–1.44)	81 (44.3)	0.73 (0.51–1.07)	0.87 (0.57–1.33)

adjusting for: sex, age, high educational level, smoker, b/tsDMARDbiologic or targeted synthetic disease-modifying antirheumatic drug, csDMARDconventional synthetic disease-modifying antirheumatic drug, corticosteroid.; ref., reference. cDAPSA-remission, clinical Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSA-remission, Disease Activity for Psoriatic Arthritis (DAPSA-remLDA, DAPSA) remission; DAPSA-remLDA, DAPSA remission or low disease activity; DAS28-remission, 28-joint Disease Activity Score remission; MDA, Minimal Disease Activity; n, number; OR, odds ratio adjusting for: sex, age; ORadj,

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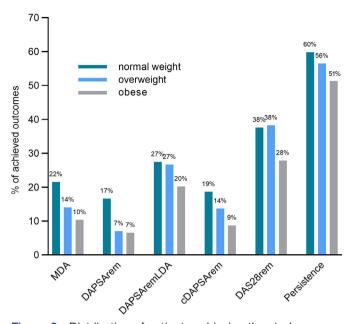


Figure 2 Distribution of patients achieving the study primary and secondary outcomes within the first year, and percentage of patients achieving treatment persistence at the end of month 12, stratified by body mass index category. cDAPSArem, clinical Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSArem, DAPSA remission; DAPSA-remLDA, DAPSA remission or low disease activity; DAS28rem, 28-joint Disease Activity Score remission; MDA, Minimal Disease Activity.

association with achievement of DAPSA-remLDA within the first year and with 1-year treatment persistence, were not statistically significant. Among patients who achieved MDA, the majority also achieved cDAPSA-remission.

Our findings on the association between obesity and lower probability of reaching MDA and remission are consistent with other longitudinal observational studies. 10 13 15 In the prospective study by Di Minno et al. obesity was associated with increased risk of not achieving MDA during a 12 months follow-up compared with patients with BMI  $<30 \text{ kg/m}^2$  (HR 4.90, 95% CI 3.04 to 7.87). 13 Eder et al reported that, compared with normal weight patients (BMI <25 kg/m<sup>2</sup>), overweight patients and patients with obesity had 34% and 47% significantly reduced odds of achieving MDA, respectively. While we identified a similar OR in the overweight patients and patients with obesity, our results in the overweight group were not statistically significant. In the study by Højgaard et al, obesity was associated with 53% lower odds of achieving European Alliance of Associations for Rheumatology good or moderate (EGOM) response. 15 While we did not assess EGOM response, this is a DAS28-driven outcome, and the findings are in agreement with our observed association between obesity and 49% reduced odds for DAS28-remission. Conversely, Iannone et al suggested no significant differences in DAS28-remission rates across BMI categories.<sup>26</sup> However, they had a small sample size (135 patients), and their observed lower

remission rate in the obese vs normal weight patients was in line with our findings.

Additionally, results from Højgaard *et al* showed that compared with patients without obesity (BMI <30 kg/m²), patients with obesity were associated with a 60% higher risk of TNFi discontinuation during their study period (median follow-up of 1.5 years). <sup>15</sup> While our study did not yield an association between BMI and treatment persistence, these contrasting findings may be explained by the different methodologies. Højgaard *et al* assessed the time to withdrawal using a survival model, which gives high attention to early outcomes, while we investigated persistence yes/no at a specific timepoint using logistic regression.

In our study, MDA was the main outcome as it covers several aspects from the disease presentation and consequences, and has been associated with patient's QoL and productivity.<sup>27</sup> Additionally, McGagh and Coates suggested that the 66/68 joint counts provide a more realistic picture of joint involvement in PsA, compared with the 28 joint counts, and highlighted the benefits of including patient-reported outcomes.<sup>28</sup> Based on this, we identified DAPSA-remission and cDAPSA-remission as optimal secondary outcomes. However, we expect that cDAPSA may be a better fit to study patients with abnormal BMI since obesity was associated with elevated CRP in the general population. 29-31 This is further supported by the high overlap of patients achieving MDA and cDAPSAremission in our study, which was similar across every BMI group.

Regarding the observed higher frequency of achievement of DAS28-remission compared with other remission end points, this may be explained by its narrow focus on peripheral manifestations, potentially underestimating residual disease activity. Nevertheless, the consistency of the observed results on MDA and remission outcomes in the obese group suggests that obesity affects peripheral joints, as well as disease-specific manifestations and the patient's perspective. However, we note that the different outcome definitions led to contrasting results in the overweight group, suggesting that the effect of overweight on the PsA may not be fully captured by every remission definition. Similarly, the impact of obesity on PsA clinical response was not consistent with the more clinically accessible outcome low disease activity (DAPSA-remLDA).

The reasons for the lower response rates in patients with obesity could be multiple. High body weight can affect the clearance and volume of distribution of b/tsDMARDs. 32-34 Adipose tissue has a proinflammatory capacity, 35 which could negatively influence drug response. Finally, a relationship between mechanical stress and triggering of musculoskeletal inflammation (deep Köbner phenomenon) in PsA is discussed. Nevertheless, the observed lower odds of achieving MDA or remission in the obese group is of interest, and the consistency across the studied definitions of remission suggests that this effect may be reflected on several factors of the PsA disease.

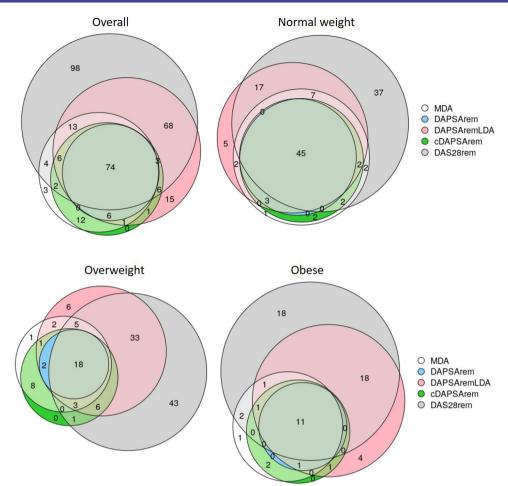


Figure 3 Venn diagram depicting the number of patients (counts) achieving the study individual primary and secondary outcomes within the first year, overall and stratifying by body mass index category. cDAPSArem, clinical Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSArem, DAPSA remission; DAPSAremLDA, DAPSA remission or low disease activity; DAS28rem, 28-joint Disease Activity Score remission; MDA, Minimal Disease Activity.

Finally, as described elsewhere, 12 the prevalence of overweight and obesity were higher among patients with PsA in comparison to the general population in Switzerland (Switzerland 2017, people >15 years old, 31% overweight and 11% obese). 36 Higher obesity prevalence among patients with PsA in comparison to the reference population was in agreement with prior studies.<sup>12</sup>

#### **Strengths and limitations**

In addition to the large sample size and availability of BMI information (often lacking in real-world data), the key strength of this study is the use of several relevant clinical outcome definitions. While multiple approaches to assess PsA disease activity exist, no single one has been identified as sufficient<sup>37</sup> and the choice of the optimal measure remains challenging.<sup>28</sup> The consistency of the observed results on MDA and remission outcomes in the obese group reinforces the study findings. However, we did not look at unidimensional outcomes (eg. dactylitis) and this remains of interest for future studies. Additionally, while standard MDA definition includes Psoriasis Activity and Severity Index ≤1 or body surface area ≤3,38 due to data restrictions our MDA definition included a skin

manifestation of 'none' or 'almost none', as reported by the physician.

We did not require a minimum time between treatment start and outcome record. In a post hoc test, we identified that the median time to the record for MDA assessment was between 214 and 245 days, similar across the BMI groups. Additionally, patients could have records of the outcome variable(s) at more than one visit during follow-up. When more than one record was available, all were assessed to identify if successful outcome was achieved.

Intrinsic to real-world data, missingness was a limitation. We addressed missingness at baseline with multiple imputation and missingness during follow-up with sensitivity analyses. Our results were mainly consistent among various sensitivity analyses. For example, the secondary analysis excluding patients who missed information on the outcome during follow-up (instead of treating them as non-achievers of the respective outcome), supported the observed effect of obesity towards MDA and remission, which was even accentuated in this sensitivity analysis. Among secondary analyses varying the duration of follow-up, the 15-month analyses showed consistence with the main findings, and the reduced effect found in the 9-month analyses may be explained by higher missingness of outcome information at shorter follow-up, and therefore lower number of observed events overall.

Limitations to consider when interpreting the results include the potential misclassification of patients in the BMI categories. While overweight and obesity are commonly defined by BMI, <sup>39 40</sup> this lacks information on body composition. Thus, although data on waist circumference, skinfold thickness and bioelectrical impedance may provide a better patient classification, this information is extremely limited in real-world data. Additionally, we classified patients with BMI <25 kg/m<sup>2</sup> as normal weight, including patients with BMI <18.5 kg/m<sup>2</sup>, who may be classified as underweight. This was done due to low prevalence of underweight patients with PsA in SCQM<sup>12</sup> and is consistent with previous practice in PsA10 26 and other inflammatory rheumatic diseases research in which the majority of studies combine normal and underweight patients.41

It was suggested that patients with obesity may benefit from other non-TNFi b/tsDMARDs, however, the evidence is limited. As Nevertheless, our results of a lower odds of achieving remission may be largely driven by the high TNFi use in our cohort.

Finally, since weight loss in overweight patients and patients with obesity was identified as a predictor of MDA achievement,<sup>20</sup> it remains of interest to perform a similar study to this one but stratifying the overweight patients and patients with obesity by those with and without weight loss.

#### CONCLUSION

This study suggests that obesity in patients with PsA is associated with at least a 50% reduction in the likelihood of achieving MDA or remission within the first year after starting b/tsDMARD therapy, when compared with normal weight patients. The consistency of findings across definitions of remission suggests that obesity affects several factors of PsA disease. Conversely, obesity was neither associated with the likelihood of achieving low disease activity nor with treatment persistence. Finally, comparative analyses of b/tsDMARDs within BMI groups is of interest and investigating the benefits of losing weight in this population remains of interest.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study was reviewed by the ethics commission of the Canton of Zurich (KEK: Req-2020-00045). Pseudonymised data, without access to the code key, was provided by the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry to the researchers. Therefore, the commission waived the need for a full ethics authorisation. Prior enrolment at SCQM, signed informed consent was provided by the patients, in accordance with the Declaration of Helsinki. Additionally, withdrawal of participation is possible at any time.

Provenance and peer review Not commissioned; externally peer reviewed.

**Data availability statement** Data may be obtained from a third party and are not publicly available. Data belong to the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) and are available only with the approval and permission from the license holder (SCQM).

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### Supplementary material

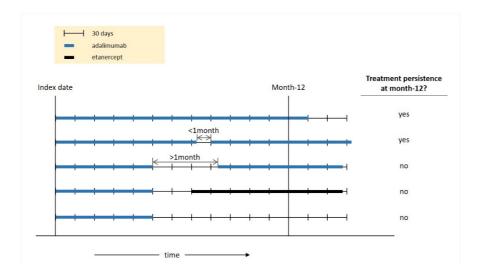
# Minimal Disease Activity and remission in psoriatic arthritis patients with elevated body mass index: an observational cohort study in the Swiss Clinical Quality Management cohort

Enriqueta Vallejo-Yagüe<sup>1</sup>, Theresa Burkard<sup>1</sup>, Raphael Micheroli<sup>2</sup>, Andrea M. Burden<sup>1</sup>

#### **Supplementary Equations**

- (1)  $BMI = \frac{weight Kg}{h cight m^2}$
- (2) DAPSA = sjc66 + tjc68 + PatActivity + PatPain + CRP
- (3) cDAPSA = sjc66 + tjc68 + PatActivity + PatPain
- (4)  $DAS28ESR = (0.56 \times \sqrt{tjc28} + 0.28 \times \sqrt{sjc28} + 0.7 \times ln(ESR)) \times 1.08 + 0.16$
- (5)  $DAS28CRP = (0.56 \times \sqrt{tjc28} + 0.28 \times \sqrt{sjc28} + 0.36 \times ln(CRP + 1)) \times 1.10 + 1.15$

Abbreviations used in the above equations: DAPSA disease activity in psoriasis arthritis score; cDAPSA clinical DAPSA; DAS28 disease activity score 28; sjc66 number of swollen joints, counting 66; sjc28 number of swollen joints, counting 28; tjc68 number of tender joints, counting 68; tjc28 number of tender joints, counting 28; CRP C-reactive protein (mg/dL); ESR erythrocyte sedimentation rate (mm/h); PatActivity patient's assessment of disease activity (0 very well - 10 very poor); PatPain patient's joint pain (0 very well - 10 very poor).



**Supplementary Figure S1.** Graphical representation of the assessment of treatment persistence at month-12 for an example patient who starts adalimumab as first biologic or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD).

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#### **Supplementary Text S1.** Additional information on covariates.

High education was defined as 'höhere Fachschule' (university of applied sciences), or 'Universitätsstudium' (university study); and the no category for this variable was defined by 'obligatorische Schule' (compulsory school), 'Berufslehre' (apprenticeship), or 'Maturitätsschule' (3-4 year high school that enables direct admission to Universities school)'.

Smoker (ever smoker) was defined by at least one record of smoker prior index date.

Patient and physician assessments on disease activity, pain, or skin manifestations, as well as medication, disease specific manifestations (musculoskeletal manifestations, dactylitis, enthesitis, sacrolitis, spinal involvement, coxitis, peripheral arthritis, nail manifestations) and comorbidities are recorded as specific variables in SCQM.

Information on comorbidities was extracted from the SCQM health issues dataset or table, which contains patient reported information. Lack of disease or health issue was assumed unless otherwise stated. Cardiovascular event/disease included cerebrovascular disease, coronary heart disease, deep vein thrombosis, heart infarct, heart insufficiency, peripheral vascular disease, pulmonary embolism, hypertension, hypotension, other cardiovascular disease, and other heart disease, ever before the index date. Diabetes included type I and type II, ever before index date. Other metabolic problems included adrenal disease, thyroid disease, diseases of other endocrine glands, dysfunctions of water electrolyte balance or acid alkaline balance, hyperlipidaemia, and hyperuricemia, within the 6-months prior index date. Depression/anxiety includes depression and anxiety, within the 6-months prior index date.

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Supplementary Table S1. Variables included in the multiple imputation.

Variable	Version 1 Included	Version 2 Included	Predicted	Predictor	Method	Missingness	Levels	Range
Outcome <sup>a</sup>	yes	-	-	yes	-	-	yes; no.	-
(MDA/DAPSArem/DAPSAremLDA/Persistence)								
Outcome <sup>a</sup> (DAS28rem)	-	yes	-	yes	-	-	yes; no.	-
Patient ID	yes	yes	-	-	-			1-774
BMI category	yes	yes	-	-	-	-	normal weight; overweight; obese.	-
BMI kg/m²	yes	yes	-	yes	-	-	-	16.56 - 51.42
Sex	yes	yes	-	yes	-	-	female (women); male (men).	-
Age	yes	yes	-	yes	-	-	-	18.37 - 84.65
Disease duration, years	yes	yes	yes	yes	pmm	17 (2.20)	-	0.04 - 47.31
High education	yes	yes	yes	yes	logreg	146 (18.86)	yes; no.	
ESR mm/h	yes	yes	yes	yes	pmm	105 (13.57)	-	1 - 110
CRP mg/dL	yes	yes	yes	yes	pmm	127 (16.41)	-	0 - 11.10
Physician's global disease activity (0-10)	yes	yes	yes	yes	pmm	31 (4.01)	-	0 - 9
Physician's global skin manifestation	yes	yes	yes	yes	polyreg	61 (7.88)	none; almost none; mild; mild to moderate; moderate; moderate to severe; severe.	-
Patient's assessment on disease activity	yes	yes	yes	yes	pmm	185 (23.90)	-	0 - 10
(0-10) (PatActv)								
Patient's joint pain (0-10) (PatPain)	yes	yes	yes	yes	pmm	174 (22.48)	-	0 - 10
Number of swollen joints 28 (sjc28)	yes	yes	yes	yes	pmm	20 (2.58)	-	0 - 22
Number of swollen joints 66 (sjc66)	yes	yes	yes	yes	pmm	72 (9.30)	-	0 - 48
Number of tender joints 28 (tjc28)	yes	yes	yes	yes	pmm	28 (3.62)	-	0 - 28
Number of tender joints 68 (tjc68)	yes	yes	yes	yes	pmm	73 (9.43)	-	0 - 68
DAPSA	yes	-	yes	yes <sup>b</sup>	passive imputation <sup>d</sup>	298 (38.5)	-	0.10 - 121
DAS28	-	yes	yes	yes <sup>c</sup>	passive imputation <sup>e</sup>	99 (12.79)	-	0.20 - 7.60
HAQ (0-3)	yes	yes	yes	yes	pmm	167 (21.58)	-	0 - 3
SF-12mcus (0-100)	yes	yes	yes	yes	pmm	206 (26.61)		18.74-67.78
SF-12pcus (0-100)	yes	yes	yes	yes	pmm	206 (26.61)		16.74-61.25
b/tsDMARD	yes	yes	-	yes	-	-	TNFi biologic; other biologic; tsDMARD.	-
csDMARD at index	yes	yes	-	yes	-	-	yes; no.	-
Prednisone at index	yes	yes	-	yes	-		yes; no.	-
Dactylitis	yes	yes	-	yes	-	-	yes; no.	-
Sacroilitis	yes	yes	-	yes	-	-	yes; no.	-
Enthesitis	yes	yes	-	yes	-	-	yes; no.	-
Spinal involvement	yes	yes	-	yes	-	-	yes; no.	-
Coxitis	yes	yes	-	yes	-	-	yes; no.	-
Dactylitis	yes	yes	-	yes	-	-	yes; no.	-

Abbreviations: BMI body mass index; ESR erythrocyte sedimentation rate; CRP C-reactive protein; PsA psoriasis arthritis; MDA Minimal Disease Activity; DAPSA Disease Activity Index for Psoriatic Arthritis; DAS28 28-joint disease activity score; HAQ Health Assessment Questionnaire; b/tsDMARD biologic or targeted synthetic disease modifying anti-rheumatic drug; csDMARD conventional synthetic disease modifying anti-rheumatic drug; TNFi tumor necrosis factor alpha inhibitor; tsDMARD targeted synthetic disease modifying anti-rheumatic drug; pmm predictive mean matching; logit logistic regression;

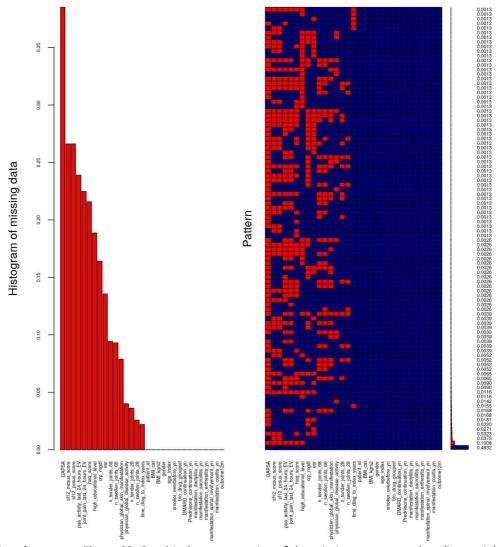
polyreg polytomous logistic regression.

<sup>o</sup> Multiple imputation was run distinctly for each outcome.

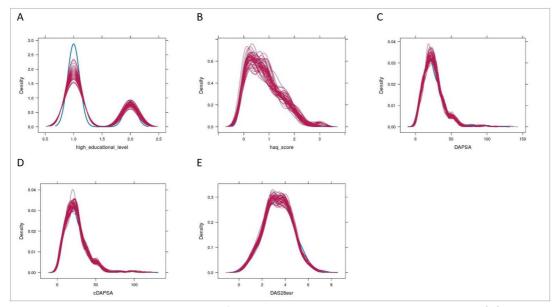
b DAPSA not used as predictor for: sjc66, tjc68, PatActivity, PatPain, CRP.

 $<sup>^{\</sup>rm d}$  DAS28 not used as predictor for: sjc28, tjc28, ESR.  $^{\rm d}$  DAPSA passive imputation: DAPSA = sjc66 + tjc68 + PatActivity + PatPain + CRP

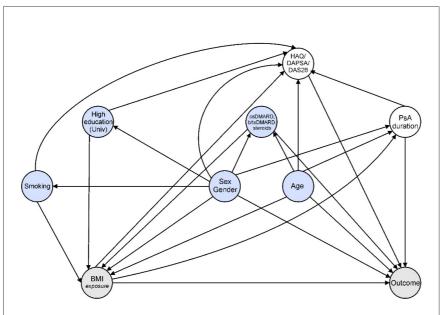
<sup>&</sup>lt;sup>e</sup> DAS28 passive imputation: DAS28ESR =  $\left(0.56 \times \sqrt{tjc28} + 0.28 \times \sqrt{sjc28} + 0.7 \times ln(ESR)\right) \times 1.08 + 0.16$ 



**Supplementary Figure S2.** Graphical representation of the missingness among baseline variables included in the imputations for primary analysis (i.e., achievement of Minimal Disease Activity (MDA) within the first year after index date). The 48.32% of patients had complete information on all the included variables. In the right figure, blue indicates availability of the data, and red missingness.

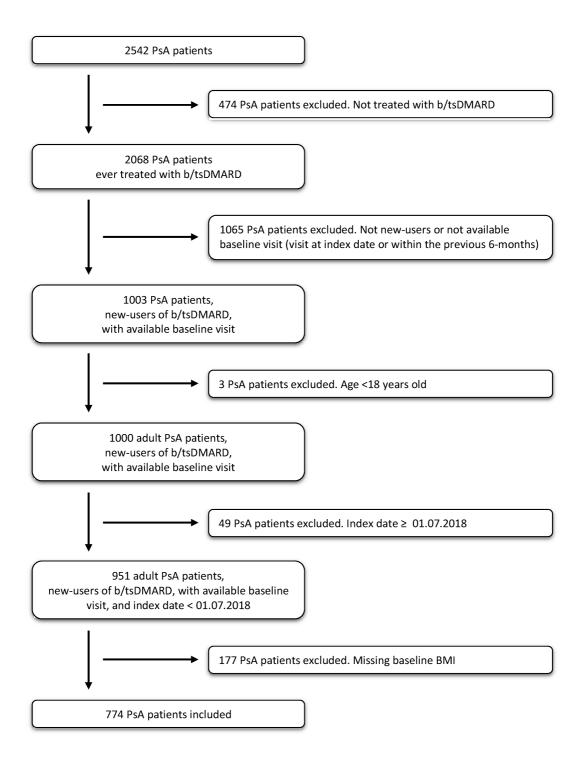


Supplementary Figure S3. Density plots for the imputed variables high educational level [A], Health Assessment Questionnaire (HAQ) [B], and Disease Activity Index for Psoriatic Arthritis (DAPSA) [C] for the primary outcome, achievement of Minimal Disease Activity (MDA) within the first year after index date. Additionally, density plot for the imputed clinical DAPSA (cDAPSA) [D] and 28-joint disease activity score (DAS28) [E] for the secondary outcomes cDAPSA-remission and DAS28-remission within the first year of treatment, respectively. The variable distribution in the original dataset is shown in blue, and the corresponding distribution in each imputed dataset is shown in red.



**Supplementary Figure S4.** Direct acyclic graph (DAG) displaying the clinical rational for selection of confounders. The nodes represent the exposure, outcome and covariates, and the lines or edges represent the assumed relationship between them. Grey nodes represent the exposure and the outcome. Blue nodes represent the confounders included in the study full adjusted model. White nodes represent other variables included in sensitivity analyses.

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**Supplementary Figure S5.** Flow chart reflecting the cohort selection based on inclusion and exclusion criteria.

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**Supplementary Table S2.** Sensitivity analyses, including the respective composite disease activity score or health standardised survey in the multivariable logistic regression of each study outcome.

		Maximum follow-up 9-months			um follow-up -months	Maximum follow-up 15-months	
	n sample size	n events	ORadj <sup>c</sup> (95% CI)	n events	ORadj <sup>c</sup> (95% CI)	n events	ORadj <sup>c</sup> (95% CI)
MDA							
Normal weight	306	45 (14.7)	1 (ref.)	66 (21.6)	1 (ref.)	86 (28.1)	1 (ref.)
Overweight	285	21 (7.4)	0.67 (0.35-1.29)	40 (14.0)	0.69 (0.42-1.15)	61 (21.4)	0.85 (0.54-1.36)
Obese	183	12 (6.6)	0.47 (0.19-1.14)	19 (10.4)	0.48 (0.25-0.96)	30 (16.4)	0.72 (0.4-1.27)
DAPSA-remission							
Normal weight	306	31 (10.1)	1 (ref.)	51 (16.7)	1 (ref.)	67 (21.9)	1 (ref.)
Overweight	285	11 (3.9)	0.7 (0.29-1.72)	20 (7.0)	0.56 (0.28-1.1)	31 (10.9)	0.6 (0.33-1.08)
Obese	183	8 (4.4)	0.78 (0.28-2.17)	12 (6.6)	0.49 (0.22-1.1)	17 (9.3)	0.49 (0.24-1)
DAPSA-remLDA							
Normal weight	306	47 (15.4)	1 (ref.)	84 (27.5)	1 (ref.)	117 (38.2)	1 (ref.)
Overweight	285	37 (13.0)	0.91 (0.48-1.75)	76 (26.7)	1.03 (0.63-1.69)	104 (36.5)	0.79 (0.5-1.25)
Obese	183	22 (12.0)	0.87 (0.41-1.85)	37 (20.2)	0.68 (0.38-1.22)	52 (28.4)	0.62 (0.36-1.04)
cDAPSA-remission							
Normal weight	306	36 (11.8)	1 (ref.)	57 (18.6)	1 (ref.)	77 (25.2)	1 (ref.)
Overweight	285	22 (7.7)	1.04 (0.51-2.13)	39 (13.7)	0.91 (0.52-1.6)	53 (18.6)	0.78 (0.47-1.29)
Obese	183	12 (6.6)	0.72 (0.28-1.81)	16 (8.7)	0.53 (0.25-1.11)	23 (12.6)	0.57 (0.3-1.07)
DAS28-remission							
Normal weight	306	68 (22.2)	1 (ref.)	115 (37.6)	1 (ref.)	153 (50.0)	1 (ref.)
Overweight	285	64 (22.5)	1.13 (0.68-1.9)	109 (38.2)	0.93 (0.6-1.43)	140 (49.1)	0.93 (0.6-1.42)
Obese	183	29 (15.8)	0.67 (0.36-1.27)	51 (27.9)	0.62 (0.37-1.04)	70 (38.3)	0.69 (0.42-1.13)
Treatment persistence							
Normal weight	306	204 (66.7)	1 (ref.)	183 (59.8)	1 (ref.)	159 (52.0)	1 (ref.)
Overweight	285	184 (64.6)	0.92 (0.61-1.4)	161 (56.5)	0.88 (0.59-1.3)	148 (51.9)	1.04 (0.71-1.54)
Obese	183	111 (60.7)	0.92 (0.56-1.49)	94 (51.4)	0.92 (0.58-1.46)	81 (44.3)	1.04 (0.66-1.64)

ORadj<sup>E</sup>: odds ratio adjusting for: sex, age, high educational level, smoker, b/tsDMARD, csDMARD, corticosteroid, and HAQ (for MDA) or DAPSA (for DAPSA-remission/DAPSA-remission/LDA) or DAS28 (for DAS28-remission).

Abbreviations: n number; CI confidence interval; ref. reference; MDA Minimal Disease Activity; DAPSA-remission Disease Activity for Psoriatic Arthritis remission; DAPSA-remLDA Disease Activity for Psoriatic Arthritis remission or low disease activity; cDAPSA-remission clinical Disease Activity for Psoriatic Arthritis remission; DAS28-remission 28-joint disease activity score remission.

**Supplementary Table S3**. Sensitivity analysis, excluding patients without follow-up data on outcome. Multivariable logistic regression for each study outcome.

		Maximum fo	llow-up 12-months	, sensitivity analysi	s
	n sample size	n events	OR <sup>a</sup> (95% CI)	Oradj <sup>b</sup> (95% CI)	Oradj <sup>c</sup> (95% CI)
MDA					
Normal weight	130	66 (50.8)	1 (ref.)	1 (ref.)	1 (ref.)
Overweight	131	40 (30.5)	0.39 (0.23-0.66)	0.45 (0.25-0.80)	0.5 (0.26-0.93)
Obese	81	19 (23.5)	0.28 (0.15-0.53)	0.33 (0.16-0.67)	0.37 (0.17-0.81)
DAPSA-remission					
Normal weight	113	51 (45.1)	1 (ref.)	1 (ref.)	1 (ref.)
Overweight	113	20 (17.7)	0.23 (0.12-0.43)	0.25 (0.12-0.49)	0.37 (0.16-0.82)
Obese	64	12 (18.8)	0.28 (0.13-0.59)	0.31 (0.14-0.71)	0.44 (0.17-1.13)
DAPSA-remLDA					
Normal weight	113	84 (74.3)	1 (ref.)	1 (ref.)	1 (ref.)
Overweight	113	76 (67.3)	0.66 (0.37-1.19)	0.58 (0.3-1.12)	0.57 (0.26-1.29)
Obese	64	37 (57.8)	0.48 (0.25-0.92)	0.44 (0.21-0.93)	0.42 (0.17-1.04)
cDAPSA-remission					
Normal weight	124	57 (46.0)	1 (ref.)	1 (ref.)	1 (ref.)
Overweight	131	39 (29.8)	0.44 (0.26-0.75)	0.47 (0.26-0.85)	0.61 (0.31-1.21)
Obese	74	16 (21.6)	0.32 (0.16-0.63)	0.36 (0.17-0.75)	0.44 (0.19-1.04)
DAS28-remission					
Normal weight	159	115 (72.3)	1 (ref.)	1 (ref.)	1 (ref.)
Overweight	153	109 (71.2)	0.86 (0.51-1.46)	0.55 (0.3-1.01)	0.57 (0.28-1.14)
Obese	89	51 (57.3)	0.48 (0.27-0.86)	0.3 (0.15-0.6)	0.37 (0.17-0.81)

OR: odds ratio adjusting for: sex, age;

ORadj: odds ratio adjusting for: sex, age, high educational level, smoker, b/tsDMARD, csDMARD, corticosteroid.

ORadj<sup>c</sup>: odds ratio adjusting for: sex, age, high educational level, smoker, b/tsDMARD, csDMARD, corticosteroid, and HAQ (for MDA) or DAPSA (for DAPSA-remission/DAPSA-remission/LDA) or DAS28 (for DAS28-remission).

Abbreviations: n number; CI confidence interval; ref. reference; Abbreviations: n number; CI confidence interval; ref. reference; MDA Minimal Disease Activity; DAPSA-remission Disease Activity for Psoriatic Arthritis remission; DAPSA-remLDA Disease Activity for Psoriatic Arthritis remission or low disease activity; cDAPSA-remission clinical Disease Activity for Psoriatic Arthritis remission; DAS28-remission 28-joint disease activity score remission

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**Supplementary Table S4**. Sensitivity analyses, excluding the 12 patients with body mass index (BMI) <18.5 kg/m². Result from the multivariable logistic regression investigating the association between body mass index (BMI) categories and various clinical outcomes, with maximum follow-up 12-months.

Sensitivity analyses		Maximum follow-up 12-months					
(Excluding BMI<18.5)	n sample size	n vents	OR	ORadj			
MDA							
Normal weight	294	62 (21.1)	1 (ref.)	1 (ref.)			
Overweight	285	40 (14.0)	0.61 (0.39-0.95)	0.65 (0.40-1.06)			
Obese	183	19 (10.4)	0.44 (0.25-0.77)	0.45 (0.24-0.84)			
DAPSA-remission							
Normal weight	294	47 (16)	1 (ref.)	1 (ref.)			
Overweight	285	20 (7.0)	0.40 (0.23-0.70)	0.46 (0.25-0.83)			
Obese	183	12 (6.6)	0.38 (0.20-0.75)	0.43 (0.21-0.88)			
DAPSA-remLDA							
Normal weight	294	80 (27.2)	1 (ref.)	1 (ref.)			
Overweight	285	76 (26.7)	0.96 (0.66-1.40)	0.99 (0.65-1.50)			
Obese	183	37 (20.2)	0.68 (0.44-1.06)	0.70 (0.42-1.14)			
cDAPSA-remission							
Normal weight	294	294 (18)	1 (ref.)	1 (ref.)			
Overweight	285	39 (13.7)	0.72 (0.46-1.14)	0.81 (0.49-1.33)			
Obese	183	16 (8.7)	0.45 (0.25-0.81)	0.53 (0.28-1.00)			
DAS28-remission							
Normal weight	294	110 (37.4)					
Overweight	285	109 (38.2)	1.00 (0.71-1.42)	0.89 (0.61-1.31)			
Obese	183	51 (27.9)	0.65 (0.44-0.98)	0.51 (0.32-0.82)			
Treatment persistence at the end of follow-up							
Normal weight	294	179 (60.9)	1 (ref.)	1 (ref.)			
Overweight	285	161 (56.5)	0.81 (0.58-1.13)	0.83 (0.56-1.23)			
Obese	183	94 (51.4)	0.68 (0.47-0.99)	0.8 (0.52-1.24)			

OR: odds ratio adjusting for: sex, age;

ORadj: odds ratio adjusting for: sex, age, high educational level, smoker, b/tsDMARD, csDMARD, corticosteroid. Abbreviations: n number; CI confidence interval; ref. reference; MDA Minimal Disease Activity; DAPSA-remission Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSA-remLDA DAPSA remission or low disease activity; cDAPSA-remission clinical DAPSA remission; DAS28-remission 28-joint disease activity score remission.

Supplementary Table S5. Number of patients, overall and stratified by body mass index (BMI) category, for each corresponding set of achieved outcomes within the first year. These numerical values complement the Figure 4 Venn Diagram. Each patient may achieve none, one, or more outcomes. Each row includes patients with the same set of achieved outcomes. The symbol ✓ indicates that the corresponding outcome (column-wise) was achieved. Conversely, the symbol − indicates that the corresponding outcome was not achieved. To obtain the total number of patients achieving a specific outcome, every column with the corresponding outcome marked as achieved should be sum.

Α	chiev	ed out	tcome	S				
МБА	DAPSArem	DAPSAremLDA	cDAPSArem	DAS28rem	Overall (n=774) (counts)	Normal weight (n=306) (counts)	Overweight (n=285) (counts)	Obese (n=183) (counts)
√	-	-	-	-	3	1	1	1
V	-	٧	-	-	4	2	2	0
V	-	-	-	٧	4	2	0	2
V	-	٧	-	٧	13	7	5	1
V	-	-	٧	-	12	2	8	2
V	-	٧	٧	-	1	0	1	0
V	-	-	٧	٧	2	2	0	0
V	-	٧	٧	٧	6	2	3	1
V	٧	٧	٧	-	6	3	2	1
٧	٧	٧	٧	٧	74	45	18	11
-	-	٧	-	-	15	5	6	4
-	-	-	-	٧	98	37	43	18
-	-	٧	-	٧	68	17	33	18
-	-	٧	٧	-	1	0	0	1
-	-	-	٧	٧	1	0	1	0
-	-	٧	٧	٧	6	0	6	0
-	٧	٧	٧	٧	3	3	0	0

Abbreviations: MDA minimal disease activity; DAPSArem Disease Activity for Psoriatic Arthritis remission; DAPSAremLDA Disease Activity for Psoriatic Arthritis remission or low disease activity; cDAPSArem clinical Disease Activity for Psoriatic Arthritis remission; DAS28rem 28-joint disease activity score remission.