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Obesity and lower likelihood of achieving Minimal Disease Activity and remission in psoriatic arthritis patients: a cohort study

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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 PsA patients in Switzerland. Secondarily, to assess the accordance or overlapping across the study outcomes.

Methods: This observational cohort study in the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry included PsA patients starting their first biologic or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) from 1997 to 30.06.2018. 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 one-year, in overweight and obese patients compared to 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, accordance or overlapping across study outcomes was investigated.

Results: The study included 306 (39.5%) normal weight, 285 (36.8%) overweight, and 183 (23.6%) obese patients. Compared to the normal weight group, obese patients had lower odds of achieving MDA at ≤12-months (Adjusted odds ratio [ORadj] 0.45, 95% confidence interval [CI] 0.24-0.82). This was consistent with the observed reduced odds of achieving DAPSA-remission (ORadj 0.42, 95%CI 0.21-0.85), cDAPSA-remission (ORadj 0.51, 95%CI 0.27-0.96), and DAS28-remission (ORadj 0.51, 95%CI 0.32-0.81) in obese vs 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 treatment persistence across the BMI strata.

Conclusions: Obesity halved the likelihood of achieving MDA and remission in PsA patients with b/tsDMARDs compared to those with normal weight, while it did not impact treatment persistence.

Strengths and limitations of this study

- ► This study uses an optimal data source, the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM), which is a nationwide rheumatology registry including data on patient characteristics, clinical features and medication. This enables to well capture the study exposure, outcome, and relevant covariates.
- ► However, while overweight and obesity are commonly defined by body mass index (BMI) thresholds, we acknowledge that using BMI without additional information on waist circumference or other measures of body composition may lead to a potential misclassification of patients.
- ► We used multiple imputation to complete baseline variables relevant for the statistical analyses.
- ► In cohort studies, different outcome definitions aiming to assess the same clinical feature (e.g., improvement) could lead to different results. This study includes several definitions of successful clinical outcome, which allows for a better understanding and discussion of the study findings. However, we did not investigate unidimensional outcomes (e.g., dactilytis).
- ► The study included sensitivity analyses to investigate methodological assumptions.

INTRODUCTION

Psoriatic arthritis (PsA) is an immune-mediated rheumatic disease,[1] with an estimated prevalence of 0.05-0.42%,[2–4] and 5-41% among patients with psoriasis.[3] PsA is a complex and multifactorial disease,[5] 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.[6] Pharmacological treatments include conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) and biologic or targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs).[3] Treatment of PsA aims to maximise health-related quality of life (QoL), through targeting symptoms and structural damage,[7] and it is recommended to target low/minimal disease activity or remission.[6]

One of the most common comorbidities in PsA patients is obesity,[1,8] and higher prevalence of obesity has been reported among PsA patients (23%-37%) compared to the general population.[9–12] Among PsA patients, obesity has been associated to lower probability of achieving Minimal Disease Activity (MDA) compared to patients with normal weight.[10,13,14] Similarly, obese PsA patients treated with tumour necrosis factor alfa inhibitors (TNFi) showed higher risk of treatment discontinuation compared to non-obese patients,[15] as well as lower odds of achieving treatment response compared to non-obese[15] or normal weight patients.[16] However, Iannone et al. found no statistically significant differences in remission rates among obese and normal weight PsA patients treated with TNFis.[17] Thus, there seems to be controversy on the topic and it is unclear whether the findings would be always consistent depending on the used clinical outcome definition.

The rationale behind the association between obesity and PsA has been previously discussed.[5,18,19] In short, obesity has been described as a low-grade inflammatory disease,[19] and both obesity and PsA share pathological inflammatory pathways.[5,19,20] 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.[21] Additionally, obesity is a well-known contributor to the metabolic syndrome (MetS), and MetS was similarly associated to lower likelihood of achieving MDA in PsA patients.[22]

These findings support the need to study PsA patients with elevated BMI. Thus, we seek to contribute to the growing body of evidence by performing an observational cohort study aiming to assess the impact of BMI in the achievement of MDA and remission in PsA patients. 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 January 1st 1997 and July 31st 2019. The SCQM is a national longitudinal population-based cohort of rheumatic diseases in Switzerland, initiated in 1997.[23] SCQM data are recorded during routine clinical practice, and includes information on demographics, body height and weight, life-style habits, anti-rheumatic medication (with start and stop dates), clinical endpoints, patient-reported outcomes, and fragility and health standardized surveys.[12,23]

Study population

PsA patients (≥18 years old) starting their first b/tsDMARD in the SCQM registry between January 1st 1997 and June 30th 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/m^2) was calculated using height and weight records (**Supplementary Equation 1**) at index date or as close as possible to this date within a 6-month look-back window. Patients were classified based on BMI as normal weight (BMI <25), overweight (BMI 25.0-29.9), and obese (BMI ≥30). 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) ≤1; number of swollen joint counts (SJC) ≤1; skin manifestation none or almost none; patient's joint pain by visual analogue scale (VAS, 0-100) ≤15; patient's assessment on PsA activity by VAS ≤20; Health Assessment Questionnaire (HAQ) ≤0.5; enthesis points ≤1.[24]

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 **Supplementary 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 one-month between treatment courses of the same b/tsDMARD, as illustrated in the **Supplementary Figure S1**.

Patients with missing information on the study outcomes during the follow-up were categorized 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, anti-rheumatic medication (i.e., b/tsDMARD, csDMARD, corticosteroid), inflammatory markers, physician's assessment on disease activity and skin, patient-reported disease activity and pain, joint counts, disease activity scores (i.e., DAPSA, cDAPSA, DAS28-ESR), disease-specific manifestations (i.e., musculoskeletal manifestations, dactylitis, enthesitis, sacroilitis, spinal involvement, coxitis, peripheral arthritis, nail manifestation), fragility and health standardized surveys (i.e., Health Assessment Questionnaire [HAQ], Short Form-12 [SF-12]), and comorbidities (i.e., 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 look-back window, except for: disease activity scores, disease-specific manifestations, and fragility and health surveys, which were collected with a 3-months look-back window. Information on smoking, cardiovascular event/disease, and diabetes, which was included if ever reported prior or at index date. Anti-rheumatic medication which was collected on the index date.

Data analysis

Patient baseline characteristics were described, and the overweight and obese categories were compared to the normal weight group using chi-squared test for categorical variables and t-test 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[25] in the R Statistical Software.[26] 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 **Supplementary Table S1**. The 48.32% of the study population had complete information on every variable included in the MICE for the main analysis (**Supplementary Figure S2**). Convergence of imputations was assessed by visual inspection of density plots (**Supplementary 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 (DAGs) (**Supplementary figure S4**), and included: sex, age, high education, ever smoking, and anti-rheumatic medication (i.e., b/tsDMARD, csDMARD, corticosteroid). Additionally, a sensitivity analysis was performed whereby we added the respective disease activity or fragility measurement to the fully adjusted models for primary and secondary outcomes to assess their potential mediating impact on the analyses.

Lastly, to compare accordance 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 or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

The study included 774 adult PsA patients starting their first b/tsDMARD. **Supplementary 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 to the normal weight group, overweight patients had higher SJC, were less frequently women, and had older mean age. Both overweight and obese patients had lower frequency of high education, and higher patient-reported disease activity and joint pain, while only obese patients had higher CRP levels. Compared to the normal 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 (SF-12pcs) were worse in the obese patients, and patients with obesity were more likely to have had a cardiovascular event/disease than the normal weight group.

Table 1. Patient characteristics at start of first biologic or targeted synthetic disease-modifying anti-rheumatic 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
anti-TNF biologic	279 (91.18)	262 (91.93)		160 (87.43)	
other biologic	9 (2.94)	9 (3.16)		6 (3.28)	
tsDMRAD	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/h) (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 (26.8)	57 (20)		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 (76.5)	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
Spinal involvement	81 (26.47)	70 (24.56)	0.66	40 (21.86)	0.30
Coxitis n (%))	13 (4.25)	8 (2.81)	0.47	15 (8.2)	0.11
Peripheral arthritis	141 (46.08)	138 (48.42)	0.63	94 (51.37)	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)	0.01	26.56 (14.18)	0.07
missing	118 (38.56)	103 (36.14)		77 (42.08)	
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
missing	51 (16.67)	49 (17.19)		34 (18.58)	
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)	
SF-12 pcs (mean (SD))	38.95 (10.67)	37.63 (9.71)	0.18	35.79 (9.04)	0.01
missing	77 (25.16)	78 (27.37)		51 (27.87)	

HAQ (mean (SD))	0.71 (0.66)	0.79 (0.58)	0.20	0.93 (0.61)	0.00
missing	60 (19.61)	59 (20.70)		48 (26.23)	
Cardiovascular event/disease	26 (8.50)	39 (13.68)	0.06	31 (16.94)	0.01
Diabetes or other metabolic problems	10 (3.27)	20 (7.02)	0.06	14 (7.65)	0.05
Depression/anxiety	13 (4.25)	17 (5.96)	0.45	10 (5.46)	0.69

Values are the number and column percentage, unless otherwise specified. Significance tests compare overweight or obese categories to the normal weight group using chi-squared test for categorical variables, and t-test for continuous variables, but Wilcoxon test for ESR and CRP. For these tests, missing values did not function as a grouping variable. Normal weight (BMI <25 kg/m^2); Overweight (BMI 25.0-29.9 kg/m^2); Obese (BMI≥30 kg/m^2). Abbreviations: BMI body mass index; p p-value; n sample size; SD Standard deviation; IQR Interquartile range; b/tsDMARD biologic or targeted synthetic disease-modifying anti-rheumatic drug; anti-TNF anti-tumor necrosis factor; tsDMARD targeted synthetic disease modifying anti-rheumatic drug; csDMARD conventional synthetic disease modifying anti-rheumatic drug; HLA-B27+ human leukocyte antigen B27 positive; ESR erythrocyte sedimentation rate; mm/h millimetres per hour; CRP C-reactive protein; mg/dL milligrams per decilitre; PsA psoriasis arthritis; DAPSA Disease Activity Index for Psoriatic Arthritis; DAS28 28-joint disease activity score; SF-12 Short-Form 12 health survey (SF-12); mcs mental component summary; pcs physical component summary; HAQ Health Assessment Questionnaire.

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

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-months analyses, the associations of obesity with DAPSA-remission and with cDAPSA-remission were no longer significant (**Table 2**).

Table 2. 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.

	Maximum follow-up 9-months			Maximum follow-up 15-months		
	n events	OR	ORadj	n events	OR	ORadj
MDA						
Normal weight	45	1 (ref.)	1 (ref.)	86	1 (ref.)	1 (ref.)
Overweight	21	0.47 (0.27-0.82)	0.52 (0.28-0.96)	61	0.67 (0.45-0.98)	0.75 (0.48-1.15)
Obese	12	0.41 (0.21-0.80)	0.44 (0.21-0.94)	30	0.50 (0.31-0.80)	0.57 (0.34-0.96)
DAPSA-remission						
Normal weight	31	1 (ref.)	1 (ref.)	67	1 (ref.)	1 (ref.)
Overweight	11	0.35 (0.17-0.72)	0.40 (0.18-0.88)	31	0.42 (0.26-0.68)	0.50 (0.30-0.84)
Obese	8	0.41 (0.18-0.92)	0.49 (0.20-1.18)	17	0.37 (0.21-0.67)	0.47 (0.25-0.87)
DAPSA-remLDA						
Normal weight	47	1 (ref.)	1 (ref.)	117	1 (ref.)	1 (ref.)
Overweight	37	0.81 (0.51-1.30)	0.88 (0.52-1.50)	104	0.91 (0.65-1.27)	0.90 (0.62-1.31)
Obese	22	0.75 (0.43-1.29)	0.75 (0.40-1.40)	52	0.64 (0.43-0.95)	0.66 (0.42-1.03)
cDAPSA-remission						
Normal weight	36	1 (ref.)	1 (ref.)	77	1 (ref.)	1 (ref.)
Overweight	22	0.62 (0.35-1.09)	0.70 (0.38-1.30)	53	0.65 (0.43-0.98)	0.75 (0.48-1.16)
Obese	12	0.53 (0.27-1.06)	0.64 (0.31-1.35)	23	0.43 (0.26-0.72)	0.55 (0.32-0.95)
DAS28-remission						
Normal weight	68	1 (ref.)	1 (ref.)	153	1 (ref.)	1 (ref.)
Overweight	64	1.01 (0.68-1.49)	0.91 (0.58-1.43)	140	0.91 (0.65-1.28)	0.89 (0.61-1.3)
Obese	29	0.67 (0.41-1.08)	0.50 (0.28-0.89)	70	0.62 (0.42-0.91)	0.57 (0.36-0.88)
Treatment persistence at the end of follow-up						
Normal weight	204	1 (ref.)	1 (ref.)	159	1 (ref.)	1 (ref.)
Overweight	184	0.86 (0.60-1.21)	0.91 (0.60-1.36)	148	0.96 (0.69-1.34)	0.97 (0.67-1.42)
Obese	111	0.77 (0.52-1.12)	0.91 (0.57-1.44)	81	0.73 (0.51-1.07)	0.87 (0.57-1.33)

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.

In the sensitivity analysis in which the respective disease activity or fragility measurement 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 (**Supplementary Table S2**). The sensitivity analysis excluding patients with missing information on outcome during the one-year follow-up yielded stronger reduced odds of achieving MDA and remission among abnormal BMI categories vs the normal weight group (**Supplementary Table S3**).

The frequency of achieved outcomes (with 12-months follow-up) per BMI category are presented in **Figure 2**, with the corresponding numerical values provided in **Supplementary**

Table S4. 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 obese, respectively.

The overlap of patients achieving the outcomes during the first year is illustrated in **Figure 3**, complemented with numerical values in **Supplementary Table S5**. Among the 125 patients achieving MDA (66 normal weight, 40 overweight, 19 obese), 80 also achieved DAPSA-remission, of which 48 (72.73%) were normal weight, 20 (50.00%) were overweight, and 12 (63.16%) were obese. Similarly, among patient with MDA, 54 (81.82%) normal weight, 32 (80.00%) overweight, and 15 (78.95%) obese patients 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%) obese patients.

DISCUSSION

This observational cohort study found that obese patients had a significant 49% to 58% reduced odds of achieving MDA, DAPSA-remission, cDAPSA-remission, and DAS28-remission within the first year, when compared to normal weight patients. Conversely, being overweight was only associated with a reduced odds of achieving DAPSA remission. In both high BMI categories, the association with achievement of DAPSA-remLDA within the first year and with one-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 to patients with BMI<30 (hazard ratio 4.90, 95%CI 3.04–7.87).[13] Eder et al. reported that, compared to normal weight patients

(BMI<25), overweight and obese patients had 34% and 47% significantly reduced odds of achieving MDA, respectively.[10] While we identified a similar OR in the overweight and obese patients, 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 (EULAR) 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.[17] 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 to non-obese patients (BMI<30), obese patients were associated with a 60% higher risk of TNFi discontinuation during their study period (median follow-up of 1.5 years).[15] 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. Clinicians may be inclined to continue with therapy longer in obese than in normal weight patients, given the higher disease activity at baseline and knowing that obese patients may be less likely to achieve MDA or remission. While this could impact the time to treatment stop, it may not affect the persistence at a relatively advanced time-point.

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.[27] Additionally, McGagh and Coates suggested that the 66/68 joint counts provides a more realistic picture of joint involvement in PsA, compared to the 28 joint counts, and highlighted

the benefits of including patient-reported outcomes.[28] 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 associate with elevated CRP in the general population.[29–31] This is further supported by the high overlap of patients achieving MDA and cDAPSA-remission in our study, which was similar across every BMI group.

Regarding the observed higher frequency of achievement of DAS28-remission compared to other remission endpoints, 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).

Strengths and limitations

In addition to the large sample size, 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[32] and the choice of the optimal measure remains challenging.[28] 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 (e.g., dactylitis) and this remains of interest for future studies.

Our results were mainly consistent among various sensitivity analyses. Excluding patients missing 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-months 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,[33,34] 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 as normal weight, including patients with BMI<18.5, who may be classified as underweight. This was done due to low prevalence of underweight PsA patients in SCQM[12] and is consistent with previous practice in PsA[10,17] and other inflammatory rheumatic diseases research in which the majority of studies combine normal and underweight patients.[35]

Finally, since weight loss in overweight and obese patients was identified as a predictor of MDA achievement,[21] it remains of interest to perform a similar study to this one but stratifying the overweight and obese patients by those with and without weight loss.

CONCLUSION

This study suggests that obesity in PsA patients 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 to 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.

Author Contributions

E.V.-Y., T.B., and A.M.B. contributed to the study conceptualization and methodology; E.V.-Y. performed data curation, formal analysis, visualization, and investigation; E.V.-Y. wrote the original draft manuscript, and T.B., and A.M.B. contributed with revision and editing. All authors read and agreed to the published version of the manuscript.

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Conflict of interests

None declared.

Ethics approval

This study was reviewed by the ethics commission of the Canton of Zurich (KEK: Req-2020-00045). Pseudonymized 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 authorization.

Patient consent for publication

Not required. Prior enrolment at SCQM, signed Informed Consent is provided by the patients, in accordance with the Declaration of Helsinki. Additionally, withdrawal of participation is possible at any time. Additional patient consent for publication is not required.

Data Availability Statement

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

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FIGURE LEGENDS

(Attached as JPG)

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

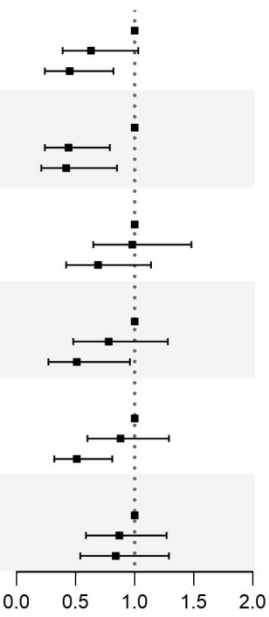
(Attached as JPG)

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 (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSAremLDA DAPSA remission or low disease activity; cDAPSArem clinical DAPSA remission; DAS28rem 28-joint disease activity score remission.

(Attached as JPG)

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 (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSAremLDA DAPSA remission or low disease activity; cDAPSArem clinical DAPSA remission; DAS28rem 28-joint disease activity score remission.

Outcome at ≤12 months unless otherwise specified	n events	OR (95% CI)	ORadj (95% CI)
MDA			
Normal weight	66	1 (ref.)	1 (ref.)
Overweight	40	0.59 (0.38-0.91)	0.63 (0.39-1.03)
Obese	19	0.43 (0.25-0.74)	0.45 (0.24-0.82)
DAPSA-remission			
Normal weight	51	1 (ref.)	1 (ref.)
Overweight	20	0.38 (0.22-0.66)	0.44 (0.24-0.79)
Obese	12	0.36 (0.19-0.70)	0.42 (0.21-0.85)
DAPSA-remLDA			
Normal weight	84	1 (ref.)	1 (ref.)
Overweight	76	0.95 (0.65-1.37)	0.98 (0.65-1.48)
Obese	37	0.67 (0.43-1.04)	0.69 (0.42-1.14)
cDAPSA-remission			
Normal weight	57	1 (ref.)	1 (ref.)
Overweight	39	0.69 (0.44-1.08)	0.78 (0.48-1.28)
Obese	16	0.43 (0.24-0.77)	0.51 (0.27-0.96)
DAS28-remission			
Normal weight	115	1 (ref.)	1 (ref.)
Overweight	109	0.99 (0.70-1.39)	0.88 (0.6-1.29)
Obese	51	0.64 (0.43-0.96)	0.51 (0.32-0.81)
Treatment persistence at the end of month-12			
Normal weight	183	1 (ref.)	1 (ref.)
Overweight	161	0.84 (0.60-1.17)	0.87 (0.59-1.27)
Obese	94	0.71 (0.49-1.03)	0.84 (0.54-1.29)



OR: odds ratio adjusting for: sex, age;

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

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..

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

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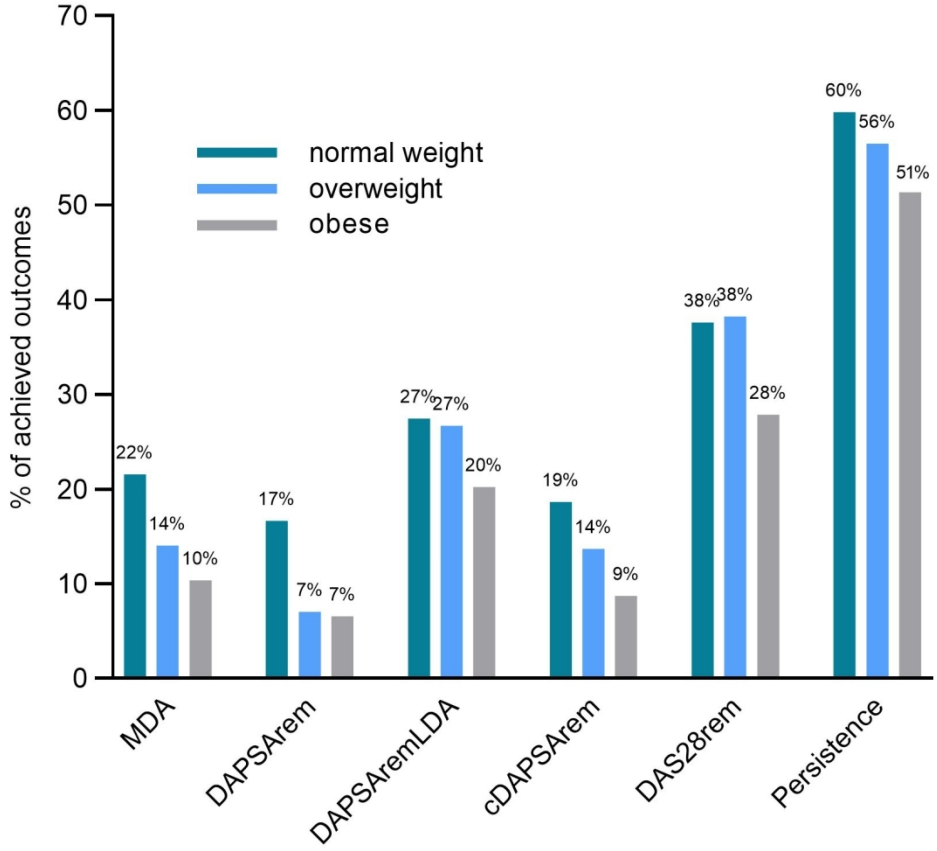

Figure 2. Distribution of patients achieving the study primary and secondary outcomes within the first year, and percentage of patients achieving treatment persistence at the end of month-12, stratified by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity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

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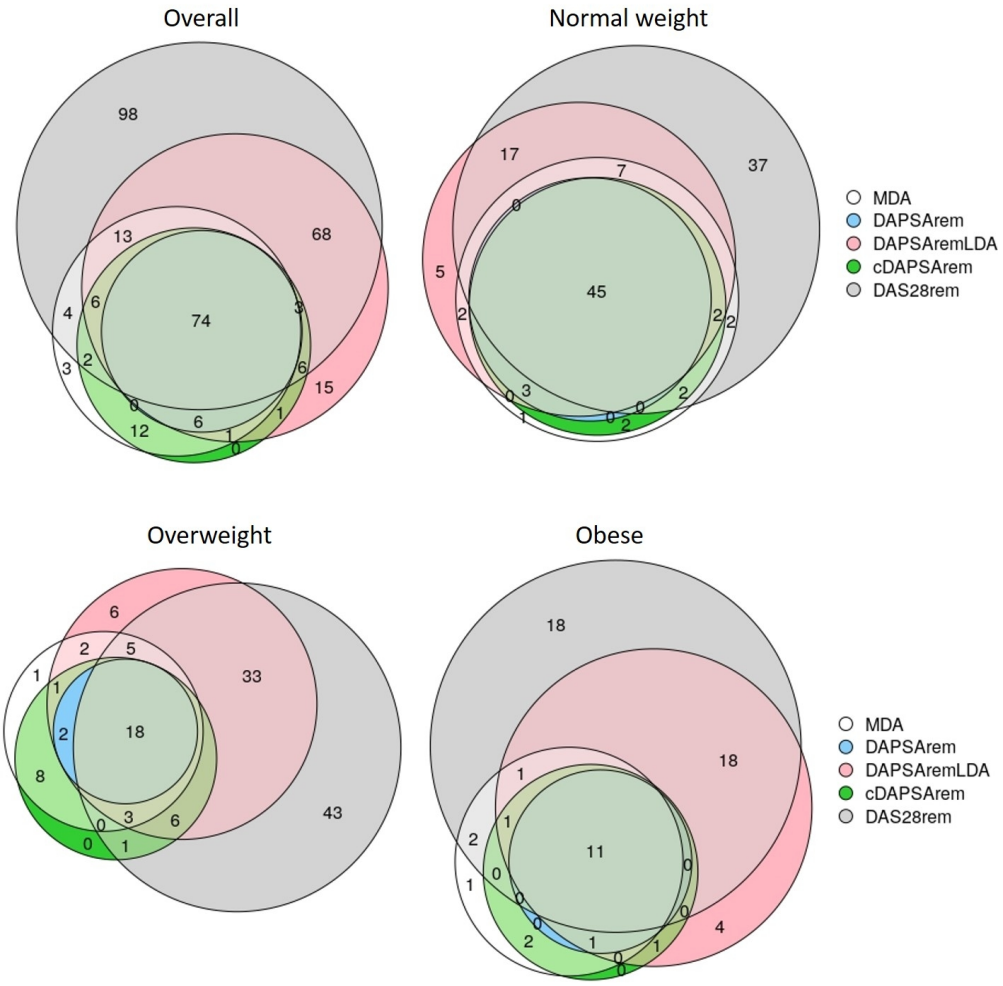

Figure 3. Venn Diagram depicting the number of patients (counts) achieving the study individual primary and secondary outcomes within the first year, overall and stratifying by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis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

238x236mm (150 x 150 DPI)

Supplementary material

Obesity and the likelihood of achieving Minimal Disease Activity and remission in psoriatic arthritis patients: a cohort study

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Supplementary Equations

(1) $BMI = \frac{weight\ Kg}{height\ m^2}$

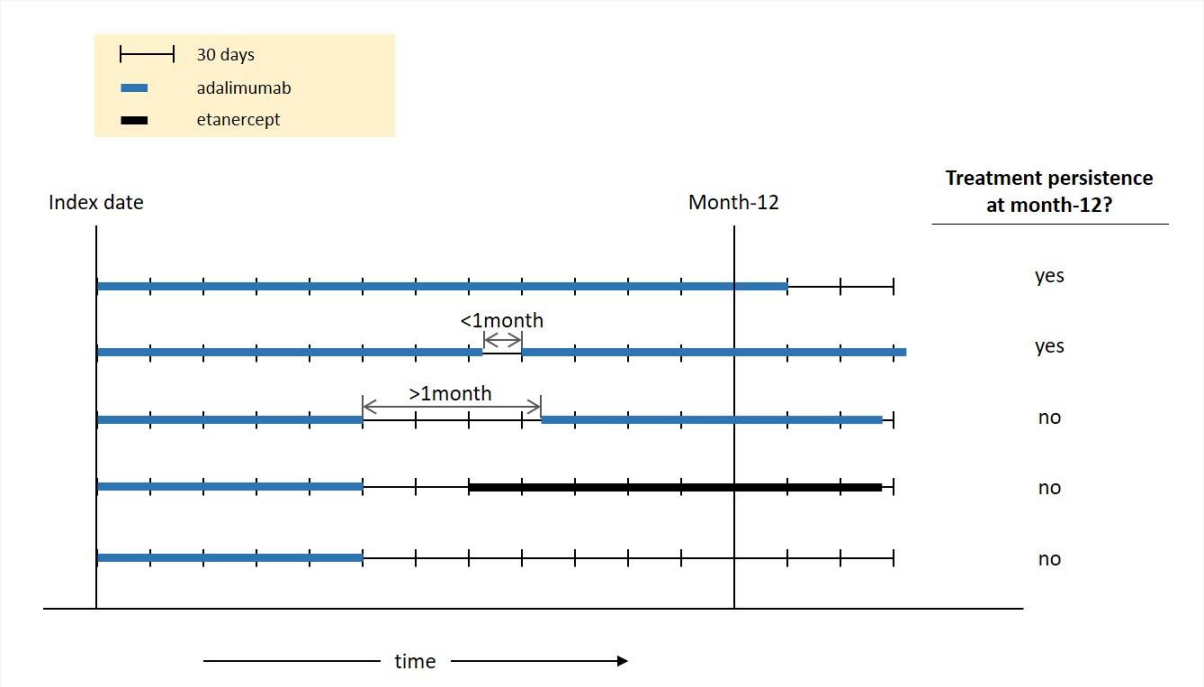
(2) $DAPSA = sjc66 + tjc68 + PatActivity + PatPain + CRP$

(3) $cDAPSA = sjc66 + tjc68 + PatActivity + PatPain$

(4) $DAS28ESR = \left(0.56 \times \sqrt{tjc28}\ + 0.28 \times \sqrt{sjc28}\ + 0.7 \times ln(ESR)\right) \times 1.08 + 0.16$

(5) $DAS28CRP = \left(0.56 \times \sqrt{tjc28}\ + 0.28 \times \sqrt{sjc28}\ + 0.36 \times ln(CRP + 1)\right) \times 1.10 + 1.15$

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).

Supplementary Table S1. Variables included in the multiple imputation.

Variable	Version 1 Included	Version 2 Included	Predicted	Predictor	Method	Missingness	Levels	Range
Outcome[a] (MDA/DAPSArem/DAPSAremLDA/Persistence)	yes	-	-	yes	-	-	yes; no.	-
Outcome[a] (DAS28rem)	-	yes	-	yes	-	-	yes; no.	-
Patient ID	yes	yes	-	-	-	-	-	1-774
BMI category	yes	yes	-	-	-	-	normal weight; overweight; obese.	-
BMI kg/m^2	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 (0-10) (PatActv)	yes	yes	yes	yes	pmm	185 (23.90)	-	0 - 10
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[b]	passive imputation[d]	298 (38.5)	-	0.10 - 121
DAS28	-	yes	yes	yes[c]	passive imputation[e]	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	-	-	anti-TNF; 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; anti-TNF anti-tumor necrosis factor; tsDMARD targeted synthetic disease modifying anti-rheumatic drug; pmm predictive mean matching; logit logistic regression; polyreg polytomous logistic regression.

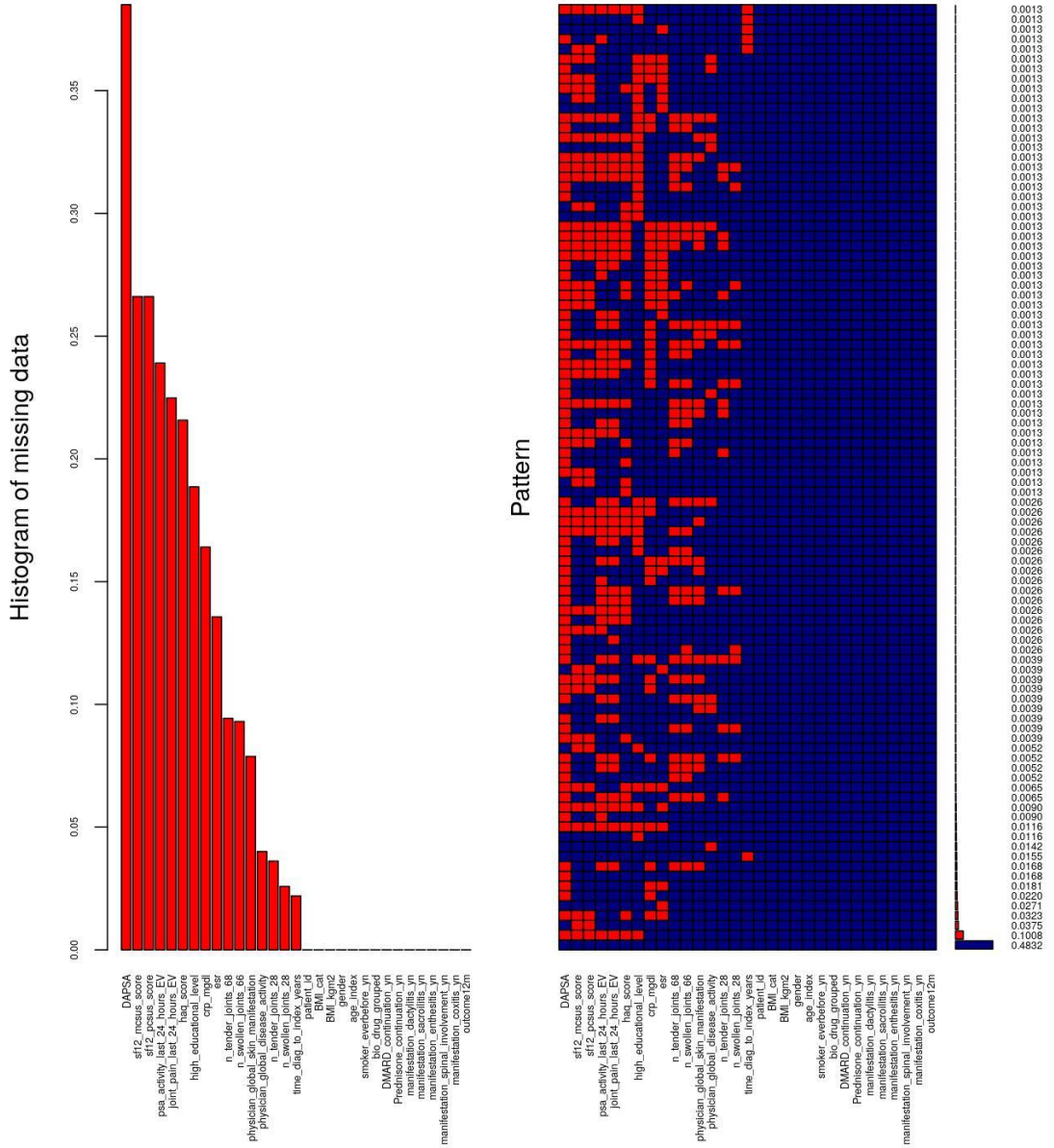
[a] Multiple imputation was run distinctly for each outcome.

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

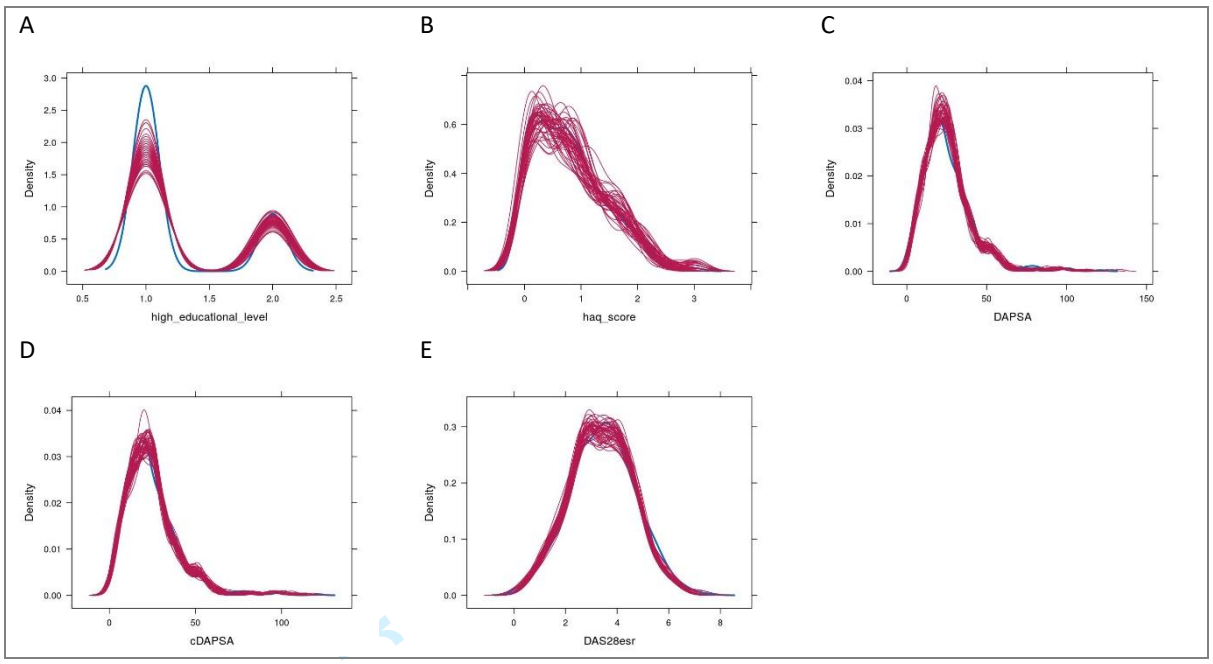
[d] DAS28 not used as predictor for: sjc28, tjc28, ESR.

[d] DAPSA passive imputation: $DAPSA = sjc66 + tjc68 + PatActivity + PatPain + CRP$

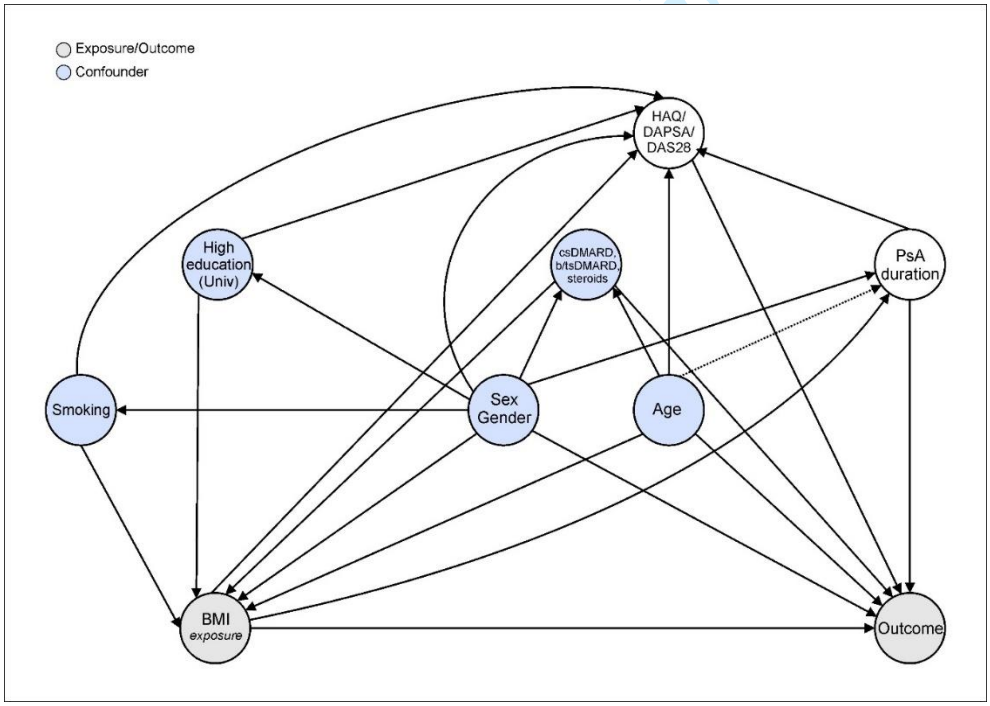
[e] DAS28 passive imputation: $DAS28ESR = \left(0.56 \times \sqrt{tjc28} + 0.28 \times \sqrt{sjc28} + 0.7 \times ln(ESR)\right) \times 1.08 + 0.16$



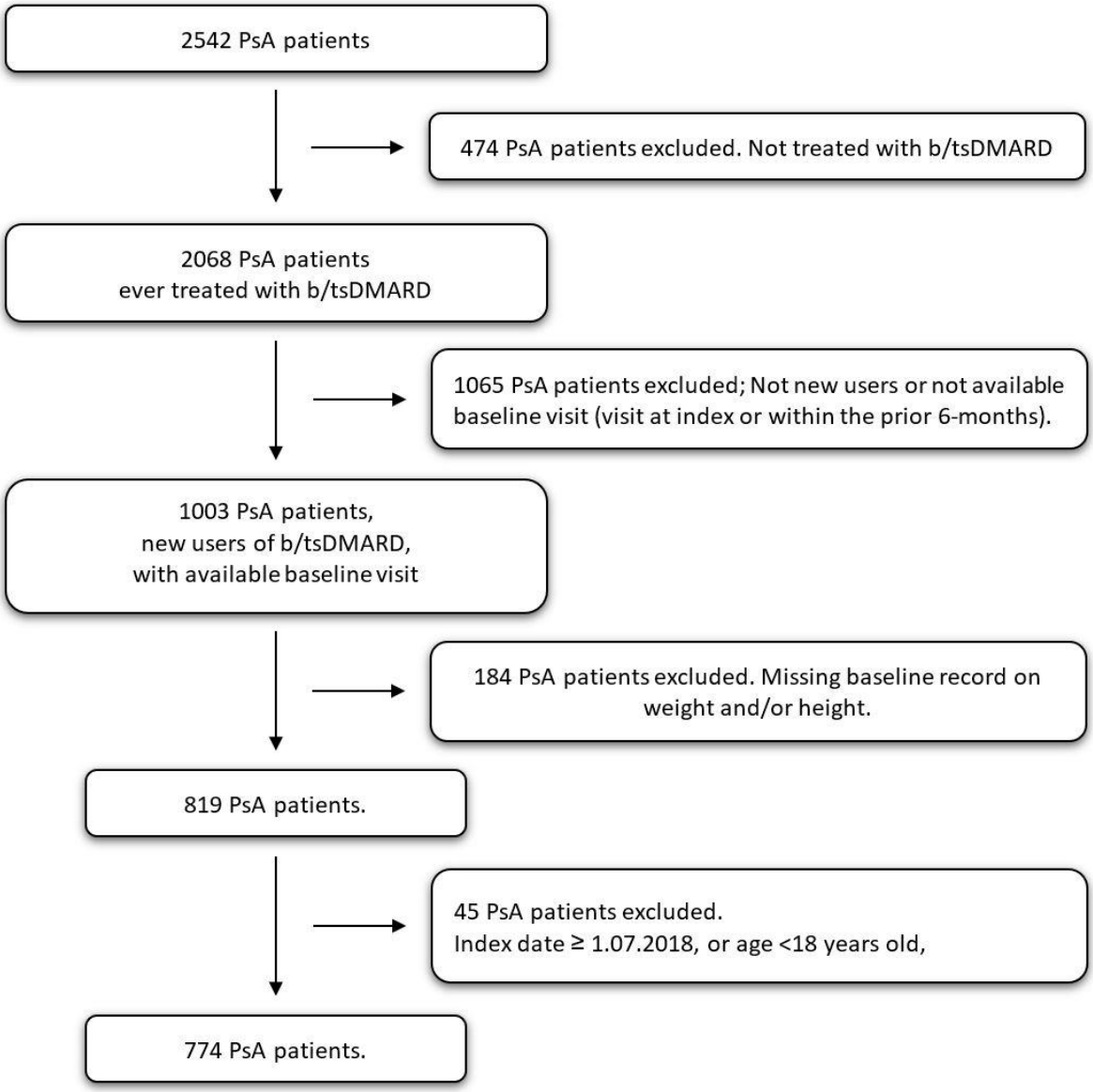
Supplementary Figure S2. Graphical representation of the missingness among baseline variables included in the imputations for primary analysis (i.e., achievement of Minimal Disease Activity (MDA) within the first year after index date). The 48.32% of patients had complete information on all the included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



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.



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

Supplementary Table S2. Sensitivity analyses, including the respective disease activity or fragility assessment in the multivariable logistic regression of each study outcome.

	Maximum follow-up 9-months		Maximum follow-up 12-months		Maximum follow-up 15-months	
	n events	ORadj[c] (95% CI)	n events	ORadj[c] (95% CI)	n events	ORadj[c] (95% CI)
MDA						
Normal weight	45	1 (ref.)	66	1 (ref.)	86	1 (ref.)
Overweight	21	0.67 (0.35-1.29)	40	0.69 (0.42-1.15)	61	0.85 (0.54-1.36)
Obese	12	0.47 (0.19-1.14)	19	0.48 (0.25-0.96)	30	0.72 (0.4-1.27)
DAPSA-remission						
Normal weight	31	1 (ref.)	51	1 (ref.)	67	1 (ref.)
Overweight	11	0.7 (0.29-1.72)	20	0.56 (0.28-1.1)	31	0.6 (0.33-1.08)
Obese	8	0.78 (0.28-2.17)	12	0.49 (0.22-1.1)	17	0.49 (0.24-1)
DAPSA-remLDA						
Normal weight	47	1 (ref.)	84	1 (ref.)	117	1 (ref.)
Overweight	37	0.91 (0.48-1.75)	76	1.03 (0.63-1.69)	104	0.79 (0.5-1.25)
Obese	22	0.87 (0.41-1.85)	37	0.68 (0.38-1.22)	52	0.62 (0.36-1.04)
cDAPSA-remission						
Normal weight	36	1 (ref.)	57	1 (ref.)	77	1 (ref.)
Overweight	22	1.04 (0.51-2.13)	39	0.91 (0.52-1.6)	53	0.78 (0.47-1.29)
Obese	12	0.72 (0.28-1.81)	16	0.53 (0.25-1.11)	23	0.57 (0.3-1.07)
DAS28-remission						
Normal weight	68	1 (ref.)	115	1 (ref.)	153	1 (ref.)
Overweight	64	1.13 (0.68-1.9)	109	0.93 (0.6-1.43)	140	0.93 (0.6-1.42)
Obese	29	0.67 (0.36-1.27)	51	0.62 (0.37-1.04)	70	0.69 (0.42-1.13)
Treatment persistence						
Normal weight	204	1 (ref.)	183	1 (ref.)	159	1 (ref.)
Overweight	184	0.92 (0.61-1.4)	161	0.88 (0.59-1.3)	148	1.04 (0.71-1.54)
Obese	111	0.92 (0.56-1.49)	94	0.92 (0.58-1.46)	81	1.04 (0.66-1.64)

ORadj[c]: 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 follow-up 12-months, sensitivity analysis				
	n sample size	n events	OR[a] (95% CI)	Oradj[b] (95% CI)	Oradj[c] (95% CI)
MDA					
Normal weight	130	66	1 (ref.)	1 (ref.)	1 (ref.)
Overweight	131	40	0.39 (0.23-0.66)	0.45 (0.25-0.80)	0.5 (0.26-0.93)
Obese	81	19	0.28 (0.15-0.53)	0.33 (0.16-0.67)	0.37 (0.17-0.81)
DAPSA-remission					
Normal weight	113	51	1 (ref.)	1 (ref.)	1 (ref.)
Overweight	113	20	0.23 (0.12-0.43)	0.25 (0.12-0.49)	0.37 (0.16-0.82)
Obese	64	12	0.28 (0.13-0.59)	0.31 (0.14-0.71)	0.44 (0.17-1.13)
DAPSA-remLDA					
Normal weight	113	84	1 (ref.)	1 (ref.)	1 (ref.)
Overweight	113	76	0.66 (0.37-1.19)	0.58 (0.3-1.12)	0.57 (0.26-1.29)
Obese	64	37	0.48 (0.25-0.92)	0.44 (0.21-0.93)	0.42 (0.17-1.04)
cDAPSA-remission					
Normal weight	124	57	1 (ref.)	1 (ref.)	1 (ref.)
Overweight	131	39	0.44 (0.26-0.75)	0.47 (0.26-0.85)	0.61 (0.31-1.21)
Obese	74	16	0.32 (0.16-0.63)	0.36 (0.17-0.75)	0.44 (0.19-1.04)
DAS28-remission					
Normal weight	159	115	1 (ref.)	1 (ref.)	1 (ref.)
Overweight	153	109	0.86 (0.51-1.46)	0.55 (0.3-1.01)	0.57 (0.28-1.14)
Obese	89	51	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[c]: 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

Supplementary Table S4. Counts and percentage of patients achieving the study outcomes (maximum follow-up 12-months), overall and stratifying by body mass index (BMI) category.

	Maximum follow-up 12-months			
	Overall (n=774)	**Normal weight** (n=306)	**Overweight** (n=285)	**Obese** (n=183)
MDA	125 (16.15)	66 (21.57)	40 (14.04)	19 (10.38)
DAPSA-remission	83 (10.72)	51 (16.67)	20 (7.02)	12 (6.56)
DAPSA-remLDA	197 (25.45)	84 (27.45)	76 (26.67)	37 (20.22)
cDAPSA-remission	112 (14.47)	57 (18.63)	39 (13.68)	16 (8.74)
DAS28-remission	275 (35.53)	115 (37.58)	109 (38.25)	51 (27.87)
Persistence	438 (56.59)	183 (59.80)	161 (56.49)	94 (51.37)

Numbers as counts and percentages (per column). Abbreviations: 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 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.

Achieved outcomes								
MDA	**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
√	-	√	-	-	4	2	2	0
√	-	-	-	√	4	2	0	2
√	-	√	-	√	13	7	5	1
√	-	-	√	-	12	2	8	2
√	-	√	√	-	1	0	1	0
√	-	-	√	√	2	2	0	0
√	-	√	√	√	6	2	3	1
√	√	√	√	-	6	3	2	1
√	√	√	√	√	74	45	18	11
-	-	√	-	-	15	5	6	4
-	-	-	-	√	98	37	43	18
-	-	√	-	√	68	17	33	18
-	-	√	√	-	1	0	0	1
-	-	-	√	√	1	0	1	0
-	-	√	√	√	6	0	6	0
-	√	√	√	√	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.

STROBE Statement

Obesity and the likelihood of achieving Minimal Disease Activity and remission in psoriatic arthritis patients: a cohort study

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2 (Title and abstract)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-9
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	5; 9; Figure 1
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	8-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	8-9
		(*d*) If applicable, explain how loss to follow-up was addressed	7
		(*e*) Describe any sensitivity analyses	7-9
Results			

Participants		13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Figure 1
			(b) Give reasons for non-participation at each stage	Figure 1
			(c) Consider use of a flow diagram	Figure 1
Descriptive data		14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
			(b) Indicate number of participants with missing data for each variable of interest	Table 1
			(c) Summarise follow-up time (eg, average and total amount)	NA (see page 7)
Outcome data		15*	Report numbers of outcome events or summary measures over time	Table 2
Main results	16		(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-11; Table 2
			(*b*) Report category boundaries when continuous variables were categorized	6 (exposure and outcome)
			(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17		Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
Discussion				
Key results	18		Summarise key results with reference to study objectives	11
Limitations	19		Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20		Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-13
Generalisability	21		Discuss the generalisability (external validity) of the study results	-
Other information				
Funding	22		Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	-

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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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

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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

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Keywords: psoriatic arthritis; minimal disease activity; remission; obesity; body mass index.

Abstract word count: 293

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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 PsA patients 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 PsA patients starting their first biologic or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) from 1997 to 30.06.2018. 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 one-year, in overweight and obese patients compared to 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, 285 (36.8%) overweight, and 183 (23.6%) obese patients. Compared to the normal weight group, obese patients had lower odds of achieving MDA at ≤12-months (Adjusted odds ratio [ORadj] 0.45, 95% confidence interval [CI] 0.24-0.82). This was consistent with the observed reduced odds of achieving DAPSA-remission (ORadj 0.42, 95%CI 0.21-0.85), cDAPSA-remission (ORadj 0.51, 95%CI 0.27-0.96), and DAS28-remission (ORadj 0.51, 95%CI 0.32-0.81) in obese vs 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 PsA patients with b/tsDMARDs compared to 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 (SCQM) is a nationwide rheumatology registry that represents one of the largest cohorts of patients with rheumatic diseases, including psoriatic arthritis (PsA).

► The availability of comprehensive patient information – including data on patient characteristics, clinical features and medication – captured the study exposure, outcome, and relevant confounders.

► Multiple definitions of the outcome could be explored, leading to a wide picture of the study findings.

► 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 axial involvement could not be studied because of the small number of patients with respective involvement.

INTRODUCTION

Psoriatic arthritis (PsA) is an immune-mediated rheumatic disease,[1] with an estimated prevalence of 0.05-0.42%,[2–4] and 5-41% among patients with psoriasis.[3] PsA is a complex and multifactorial disease,[5] 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.[6] Pharmacological treatments include conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) and biologic or targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs).[3] Treatment of PsA aims to maximise health-related quality of life (QoL), through targeting symptoms and structural damage,[7] and it is recommended to target low/minimal disease activity or remission.[6]

One of the most common comorbidities in PsA patients is obesity,[1,8] and higher prevalence of obesity has been reported among PsA patients (23%-37%) compared to the general population.[9–12] Among PsA patients, obesity has been associated to lower probability of achieving Minimal Disease Activity (MDA) compared to patients with normal weight.[10,13,14] Similarly, obese PsA patients treated with tumour necrosis factor alfa inhibitors (TNFi) showed higher risk of treatment discontinuation compared to non-obese patients,[15] as well as lower odds of achieving treatment response compared to non-obese[15] or normal weight patients.[16]

The rationale behind the association between obesity and PsA has been previously discussed.[5,17,18] In short, obesity has been described as a low-grade inflammatory disease,[18] and both obesity and PsA share pathological inflammatory pathways.[5,18,19] 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.[20] Additionally, obesity is a well-known contributor to the metabolic syndrome (MetS), and MetS was similarly associated to lower likelihood of achieving MDA in PsA patients.[21]

Despite the growing evidence on the association between obesity and worse clinical response in PsA patients, 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 PsA patients, but six of the included observational cohorts had a sample size ≤330.[16] 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 BMI in the achievement of MDA and remission in PsA patients. 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 January 1st 1997 and July 31st 2019. The SCQM is a national longitudinal population-based cohort of rheumatic diseases in Switzerland, initiated in 1997.[22] SCQM data are recorded during routine clinical practice, and includes information on demographics, body height and weight, life-style habits, anti-rheumatic medication (with start and stop dates), clinical endpoints, patient-reported outcomes, and health standardized surveys.[12,22] Diagnosis of PsA is recorded in SCQM following the physician's criteria.

Study population

PsA patients (≥18 years old) starting their first b/tsDMARD in the SCQM registry between June 1st 2020 and June 30th 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/m^2) was calculated using height and weight records (**Supplementary Equation 1**) at index date or as close as possible to this date within a 6-month look-back window. Patients were classified based on BMI as normal weight (BMI <25), overweight (BMI 25.0-29.9), and obese (BMI ≥30). 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) ≤1; number of swollen joint counts (SJC) ≤1; skin manifestation none or almost none; patient's joint pain by visual analogue scale (VAS, 0-100) ≤15; patient's assessment on PsA activity by VAS ≤20; Health Assessment Questionnaire (HAQ) ≤0.5; enthesis points ≤1.[23]

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 **Supplementary 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 one-month between treatment courses of the same b/tsDMARD, as illustrated in the **Supplementary Figure S1**.

Patients with missing information on the study outcomes during the follow-up were categorized 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, anti-rheumatic medication (i.e., b/tsDMARD, csDMARD, corticosteroid), inflammatory markers or acute phase reactants (i.e., ESR, CRP), physician's assessment on disease activity and skin, patient-reported disease activity and pain, tender and swollen joint counts (counting 28 joints), composite disease activity scores (i.e., DAPSA, cDAPSA, DAS28-ESR), disease-specific manifestations (i.e., musculoskeletal manifestations, dactylitis, enthesitis, sacroilitis, spinal involvement, coxitis, peripheral arthritis, nail manifestation), health standardized surveys (i.e., Health Assessment Questionnaire [HAQ], Short Form-12 [SF-12]), and comorbidities (i.e., 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 look-back window, except for: composite disease activity scores, disease-specific

manifestations, and health standardised surveys, which were collected with a 3-months look-back window. Information on smoking, cardiovascular event/disease, and diabetes, which was included if ever reported prior or at index date. Anti-rheumatic medication which was collected on the index date.

Data analysis

Patient baseline characteristics were described, and the overweight and obese categories were compared to the normal weight group (reference group) using chi-squared test for categorical variables and t-test, ANOVA, 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[24] in the R Statistical Software.[25] 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 **Supplementary Table S1**. The 48.32% of the study population had complete information on every variable included in the MICE for the main analysis (**Supplementary Figure S2**). Convergence of imputations was assessed by visual inspection of density plots (**Supplementary 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 (DAGs) (**Supplementary 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 standardized 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 one-year outcomes after excluding patients with underweight (BMI<18.5 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 or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

The study included 774 adult PsA patients starting their first b/tsDMARD. **Supplementary 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 to the normal weight group, overweight patients had higher SJC, were less frequently women, and had older mean age. Both overweight and obese patients had lower frequency of high education, and higher patient-reported disease activity and joint pain, while only obese patients had higher CRP levels. Compared to the normal 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 (SF-12pcs) were worse in the obese patients, and patients with obesity were more likely to have had a cardiovascular event/disease than the normal weight group.

Table 1. Patient characteristics at start of first biologic or targeted synthetic disease-modifying anti-rheumatic 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/h) (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 (26.8)	57 (20)		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 (76.5)	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
Spinal involvement	81 (26.47)	70 (24.56)	0.66	40 (21.86)	0.30
Coxitis n (%))	13 (4.25)	8 (2.81)	0.47	15 (8.2)	0.11
Peripheral arthritis	141 (46.08)	138 (48.42)	0.63	94 (51.37)	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)	0.01	26.56 (14.18)	0.07
missing	118 (38.56)	103 (36.14)		77 (42.08)	
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
missing	51 (16.67)	49 (17.19)		34 (18.58)	
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)	
SF-12 pcs (mean (SD))	38.95 (10.67)	37.63 (9.71)	0.18	35.79 (9.04)	0.01
missing	77 (25.16)	78 (27.37)		51 (27.87)	

HAQ (mean (SD))	0.71 (0.66)	0.79 (0.58)	0.20	0.93 (0.61)	0.00
missing	60 (19.61)	59 (20.70)		48 (26.23)	
Cardiovascular event/disease	26 (8.50)	39 (13.68)	0.06	31 (16.94)	0.01
Diabetes or other metabolic problems	10 (3.27)	20 (7.02)	0.06	14 (7.65)	0.05
Depression/anxiety	13 (4.25)	17 (5.96)	0.45	10 (5.46)	0.69

Values are the number and column percentage, unless otherwise specified. Significance tests compare overweight or obese categories to the normal weight group (reference) using chi-squared test for categorical variables, and t-test or ANOVA 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/m^2); Overweight (BMI 25.0-29.9 kg/m^2); Obese (BMI≥30 kg/m^2). Abbreviations: BMI body mass index; p p-value; n sample size; SD Standard deviation; IQR Interquartile range; b/tsDMARD biologic or targeted synthetic disease-modifying anti-rheumatic drug; TNFi tumor necrosis factor alpha inhibitor; tsDMARD targeted synthetic disease modifying anti-rheumatic drug; csDMARD conventional synthetic disease modifying anti-rheumatic drug; HLA-B27+ human leukocyte antigen B27 positive; ESR erythrocyte sedimentation rate; mm/h millimetres per hour; CRP C-reactive protein; mg/dL milligrams per decilitre; PsA psoriasis arthritis; DAPSA Disease Activity Index for Psoriatic Arthritis; DAS28 28-joint disease activity score; SF-12 Short-Form 12 health survey (SF-12); mcs mental component summary; pcs physical component summary; HAQ Health Assessment Questionnaire.

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

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-months analyses, the associations of obesity with DAPSA-remission and with cDAPSA-remission were no longer significant (**Table 2**).

Table 2. 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.

	n sample size	Maximum follow-up 9-months			Maximum follow-up 15-months		
		n vents	OR	ORadj	n events	OR	ORadj
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)	0.81 (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)	0.75 (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)
Obese	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)
Obese	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							
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)

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.

In the sensitivity analysis in which the respective composite disease activity score or health standardized 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 (**Supplementary Table S2**). The sensitivity analysis excluding patients with missing information on outcome during the one-year follow-up yielded stronger reduced odds of achieving MDA and remission among abnormal BMI categories vs the normal weight group (**Supplementary Table S3**). The sensitivity analysis excluding the 12 patients with BMI<18.5 yielded similar results to the main study findings **(Supplementary 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 obese, respectively.

The overlap of patients achieving the outcomes during the first year is illustrated in **Figure 3**, complemented with numerical values in **Supplementary Table S5**. Among the 125 patients achieving MDA (66 normal weight, 40 overweight, 19 obese), 80 also achieved DAPSA-remission, of which 48 (72.73%) were normal weight, 20 (50.00%) were overweight, and 12 (63.16%) were obese. Similarly, among patient with MDA, 54 (81.82%) normal weight, 32 (80.00%) overweight, and 15 (78.95%) obese patients 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%) obese patients.

DISCUSSION

This observational cohort study found that obese patients had a significant 49% to 58% reduced odds of achieving MDA, DAPSA-remission, cDAPSA-remission, and DAS28-remission within the first year, when compared to normal weight patients. Conversely, being overweight was only associated with a reduced odds of achieving DAPSA remission. In both high BMI categories, the association with achievement of DAPSA-remLDA within the first year and with one-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 to patients with BMI<30 (hazard ratio 4.90, 95%CI 3.04–7.87).[13] Eder et al. reported that, compared to normal weight patients (BMI<25), overweight and obese patients had 34% and 47% significantly reduced odds of achieving MDA, respectively.[10] While we identified a similar OR in the overweight and obese patients, 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 (EULAR) 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.[26] 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 to non-obese patients (BMI<30), obese patients were associated with a 60% higher risk of TNFi discontinuation during their study period (median follow-up of 1.5 years).[15] 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.[27] Additionally, McGagh and Coates suggested that the 66/68 joint counts provides a more realistic picture of joint involvement in PsA, compared to the 28 joint counts, and highlighted the benefits of including patient-reported outcomes.[28] 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 associate with elevated CRP in the general population.[29–31] This is further supported by the high overlap of patients achieving MDA and cDAPSA-remission in our study, which was similar across every BMI group.

Regarding the observed higher frequency of achievement of DAS28-remission compared to other remission endpoints, 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 obese patients 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 psoriatic arthritis 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.

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

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[37] and the choice of the optimal measure remains challenging.[28] 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 (e.g., dactylitis) and this remains of interest for future studies. Additionally, while standard MDA definition includes Psoriasis Activity and Severity Index (PASI) ≤1 or body surface area (BSA) ≤3,[38] due to data restrictions our MDA definition included a skin manifestation of "none" or "almost none", as reported by the physician.

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, in 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-months 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,[39,40] 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 as normal weight, including patients with BMI<18.5, who may be classified as underweight. This was done due to low prevalence of underweight PsA patients in SCQM[12] and is consistent with previous practice in PsA[10,26] and other inflammatory rheumatic diseases research in which the majority of studies combine normal and underweight patients.[41]

It was suggested that obese patients may benefit from other non-TNFi b/tsDMARDs, however, the evidence is limited.[42] 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 and obese patients was identified as a predictor of MDA achievement,[20] it remains of interest to perform a similar study to this one but stratifying the overweight and obese patients by those with and without weight loss.

CONCLUSION

This study suggests that obesity in PsA patients 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 to 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.

Author Contributions

E.V.-Y., T.B., and A.M.B. contributed to the study conceptualization and methodology; E.V.-Y. performed data curation, formal analysis, visualization, and investigation; E.V.-Y. wrote the original draft manuscript, and T.B., R.M., and A.M.B. contributed with revision and editing. All authors read and agreed to the published version of the manuscript.

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Conflict of interests

None declared.

Ethics approval

This study was reviewed by the ethics commission of the Canton of Zurich (KEK: Req-2020-00045). Pseudonymized 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 authorization.

Patient consent for publication

Not required. Prior enrolment at SCQM, signed Informed Consent is provided by the patients, in accordance with the Declaration of Helsinki. Additionally, withdrawal of participation is possible at any time. Additional patient consent for publication is not required.

Data Availability Statement

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

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FIGURE LEGENDS

(Attached as JPG)

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

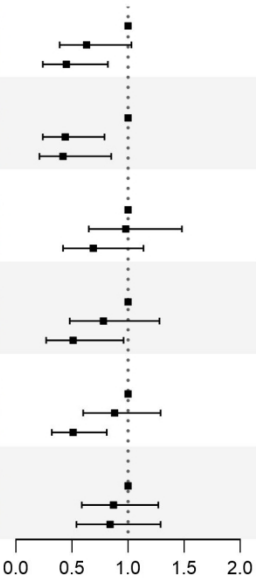
(Attached as JPG)

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 (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSAremLDA DAPSA remission or low disease activity; cDAPSArem clinical DAPSA remission; DAS28rem 28-joint disease activity score remission.

(Attached as JPG)

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 (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSAremLDA DAPSA remission or low disease activity; cDAPSArem clinical DAPSA remission; DAS28rem 28-joint disease activity score remission.

Outcome at ≤12 months unless otherwise specified	sample size, n	n (%) events	OR (95% CI)	ORadj (95% CI)
MDA				
Normal weight	306	66 (21.6)	1 (ref.)	1 (ref.)
Overweight	285	40 (14.0)	0.59 (0.38-0.91)	0.63 (0.39-1.03)
Obese	183	19 (10.4)	0.43 (0.25-0.74)	0.45 (0.24-0.82)
DAPSA-remission				
Normal weight	306	51 (16.7)	1 (ref.)	1 (ref.)
Overweight	285	20 (7.0)	0.38 (0.22-0.66)	0.44 (0.24-0.79)
Obese	183	12 (6.6)	0.36 (0.19-0.70)	0.42 (0.21-0.85)
DAPSA-remLDA				
Normal weight	306	84 (27.5)	1 (ref.)	1 (ref.)
Overweight	285	76 (26.7)	0.95 (0.65-1.37)	0.98 (0.65-1.48)
Obese	183	37 (20.2)	0.67 (0.43-1.04)	0.69 (0.42-1.14)
cDAPSA-remission				
Normal weight	306	57 (18.6)	1 (ref.)	1 (ref.)
Overweight	285	39 (13.7)	0.69 (0.44-1.08)	0.78 (0.48-1.28)
Obese	183	16 (8.7)	0.43 (0.24-0.77)	0.51 (0.27-0.96)
DAS28-remission				
Normal weight	306	115 (37.6)	1 (ref.)	1 (ref.)
Overweight	285	109 (38.2)	0.99 (0.70-1.39)	0.88 (0.6-1.29)
Obese	183	51 (27.9)	0.64 (0.43-0.96)	0.51 (0.32-0.81)
Treatment persistence at the end of month-12				
Normal weight	306	183 (59.8)	1 (ref.)	1 (ref.)
Overweight	285	161 (56.5)	0.84 (0.60-1.17)	0.87 (0.59-1.27)
Obese	183	94 (51.4)	0.71 (0.49-1.03)	0.84 (0.54-1.29)



OR: odds ratio adjusting for: sex, age;

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

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.

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

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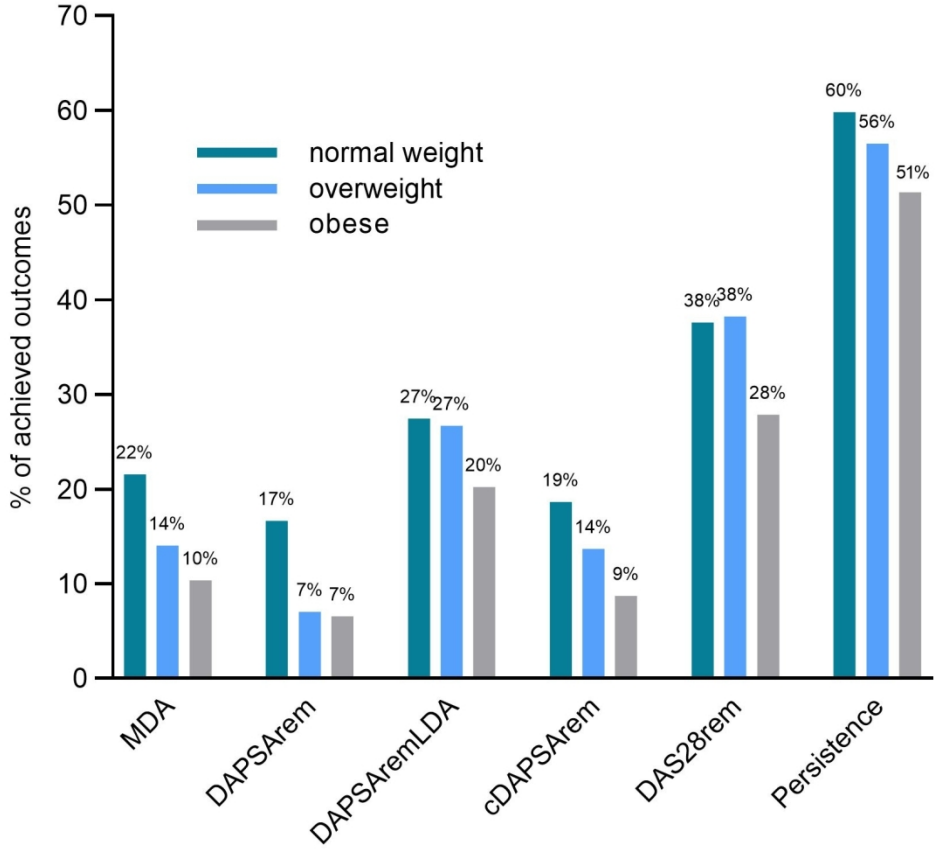

Figure 2. Distribution of patients achieving the study primary and secondary outcomes within the first year, and percentage of patients achieving treatment persistence at the end of month-12, stratified by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity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

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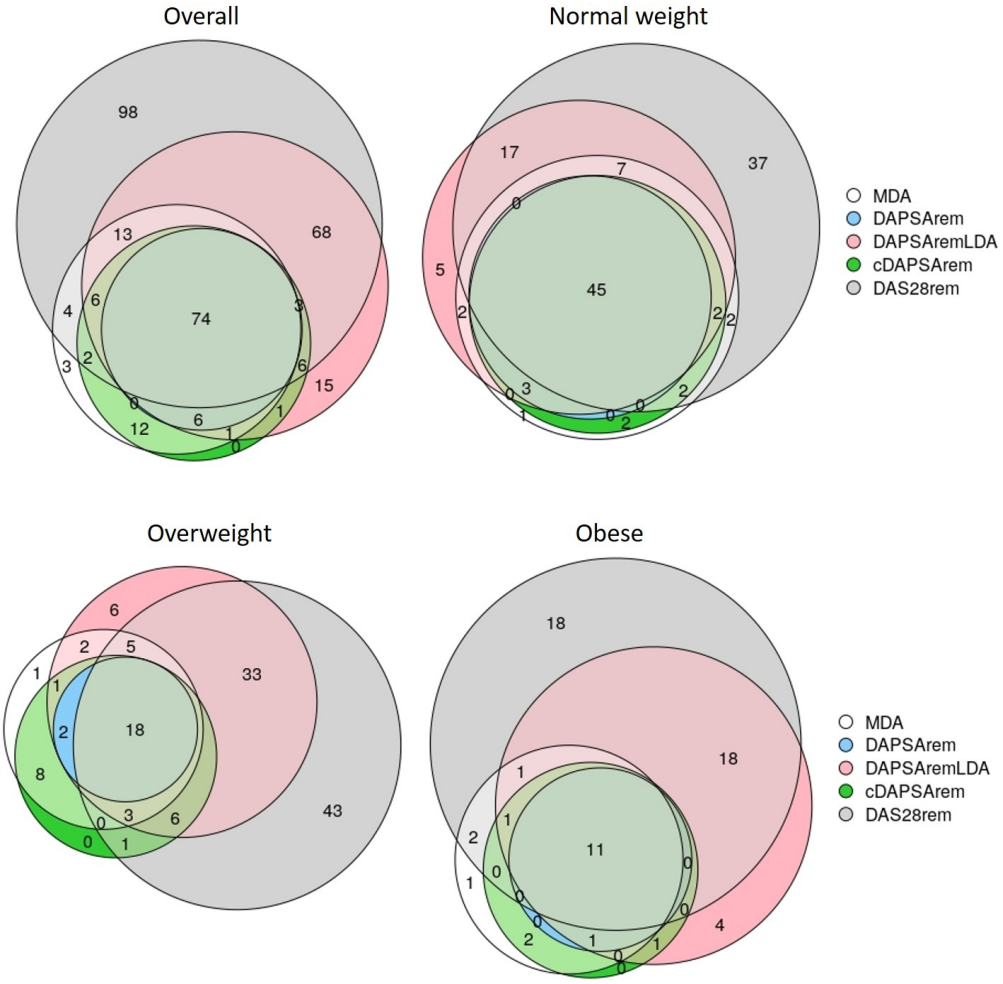

Figure 3. Venn Diagram depicting the number of patients (counts) achieving the study individual primary and secondary outcomes within the first year, overall and stratifying by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis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

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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

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Supplementary Equations

(1) $BMI = \frac{weight\ Kg}{height\ m^2}$

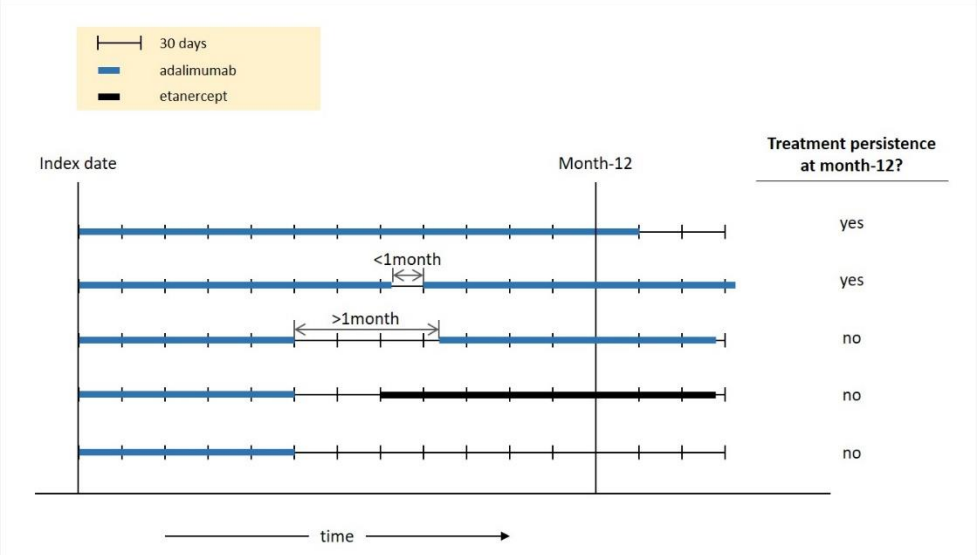
(2) $DAPSA = sjc66 + tjc68 + PatActivity + PatPain + CRP$

(3) $cDAPSA = sjc66 + tjc68 + PatActivity + PatPain$

(4) $DAS28ESR = \left(0.56 \times \sqrt{tjc28}\ + 0.28 \times \sqrt{sjc28}\ + 0.7 \times ln(ESR)\right) \times 1.08 + 0.16$

(5) $DAS28CRP = \left(0.56 \times \sqrt{tjc28}\ + 0.28 \times \sqrt{sjc28}\ + 0.36 \times ln(CRP + 1)\right) \times 1.10 + 1.15$

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).

Supplementary Table S1. Variables included in the multiple imputation.

Variable	Version 1 Included	Version 2 Included	Predicted	Predictor	Method	Missingness	Levels	Range
Outcome[a] (MDA/DAPSArem/DAPSAremLDA/Persistence)	yes	-	-	yes	-	-	yes; no.	-
Outcome[a] (DAS28rem)	-	yes	-	yes	-	-	yes; no.	-
Patient ID	yes	yes	-	-	-	-	-	1-774
BMI category	yes	yes	-	-	-	-	normal weight; overweight; obese.	-
BMI kg/m^2	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 (0-10) (PatActv)	yes	yes	yes	yes	pmm	185 (23.90)	-	0 - 10
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[b]	passive imputation[d]	298 (38.5)	-	0.10 - 121
DAS28	-	yes	yes	yes[c]	passive imputation[e]	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.

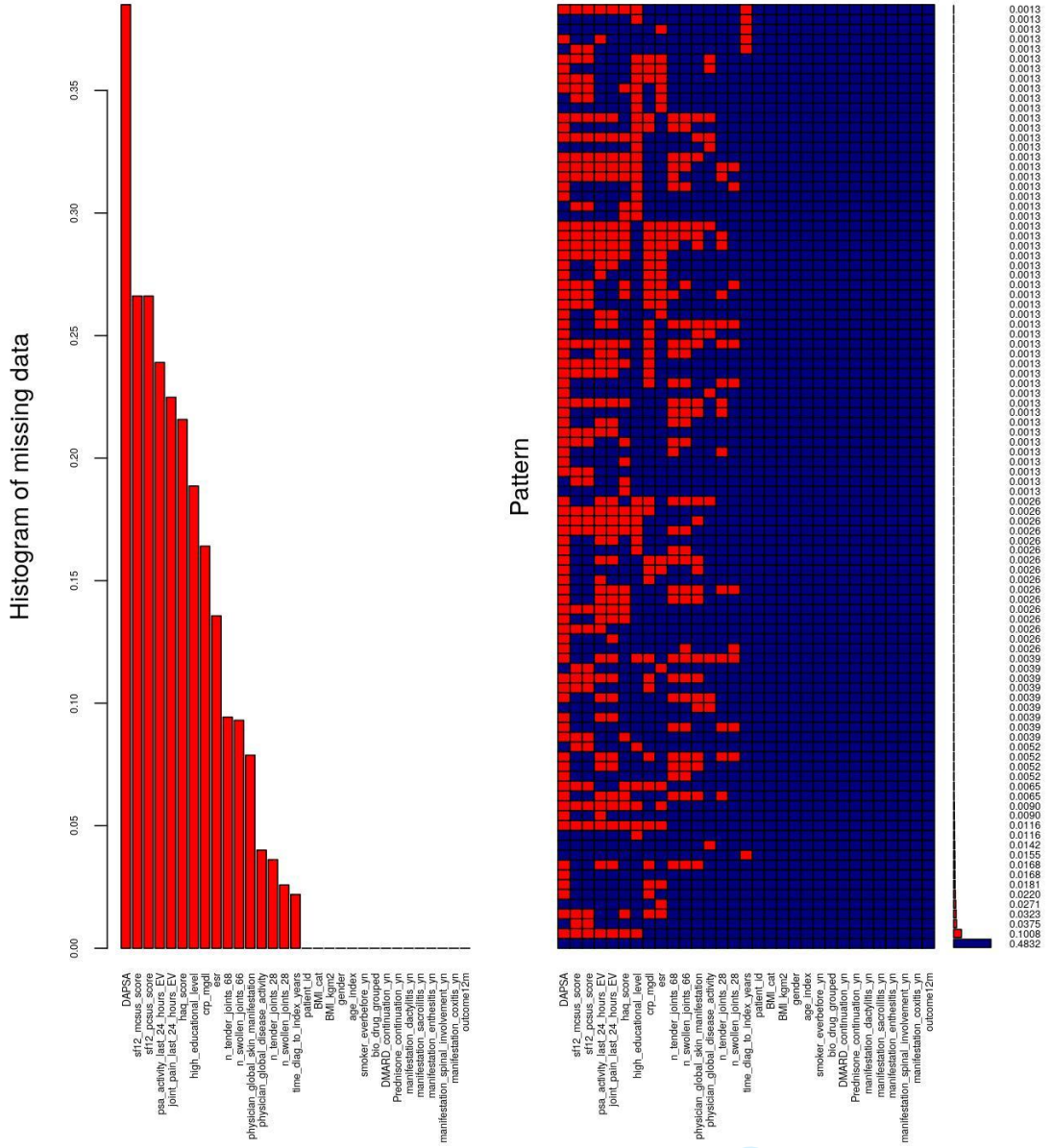
[a] Multiple imputation was run distinctly for each outcome.

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

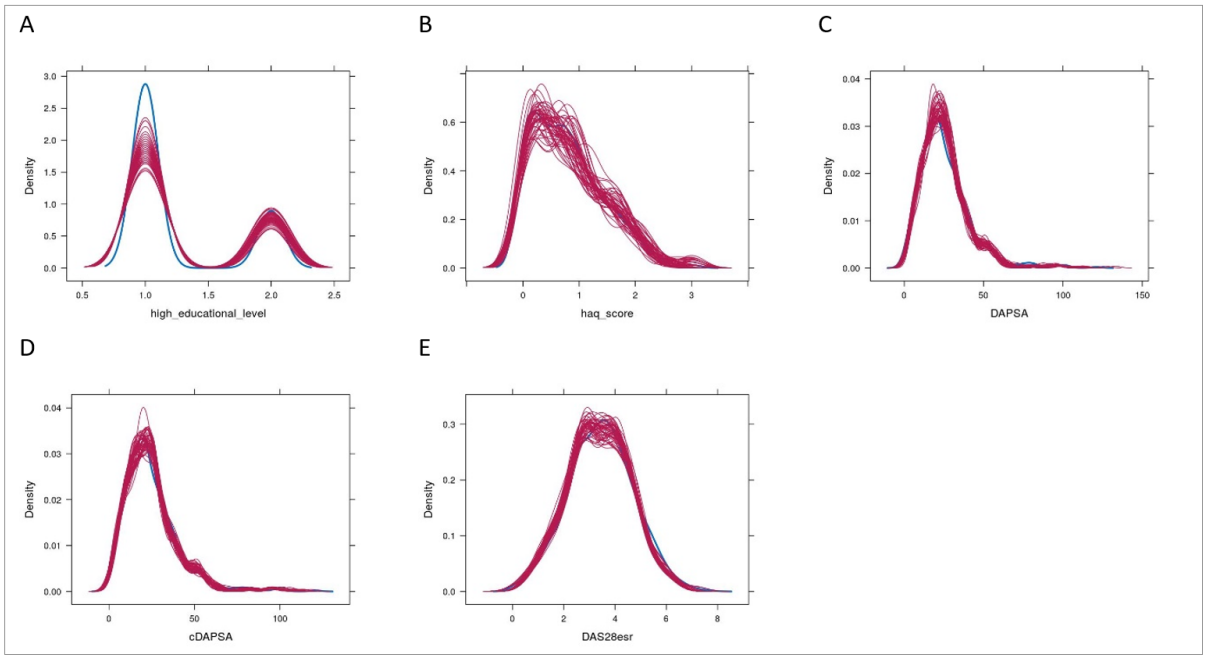
[d] DAS28 not used as predictor for: sjc28, tjc28, ESR.

[d] DAPSA passive imputation: $DAPSA = sjc66 + tjc68 + PatActivity + PatPain + CRP$

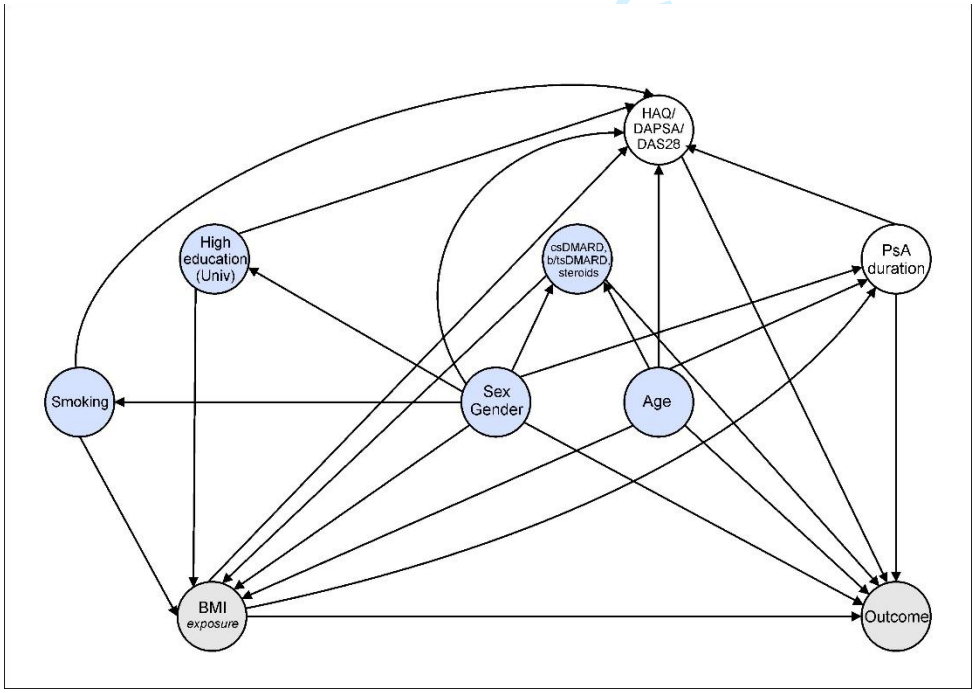
[e] DAS28 passive imputation: $DAS28ESR = \left(0.56 \times \sqrt{tjc28} + 0.28 \times \sqrt{sjc28} + 0.7 \times ln(ESR)\right) \times 1.08 + 0.16$



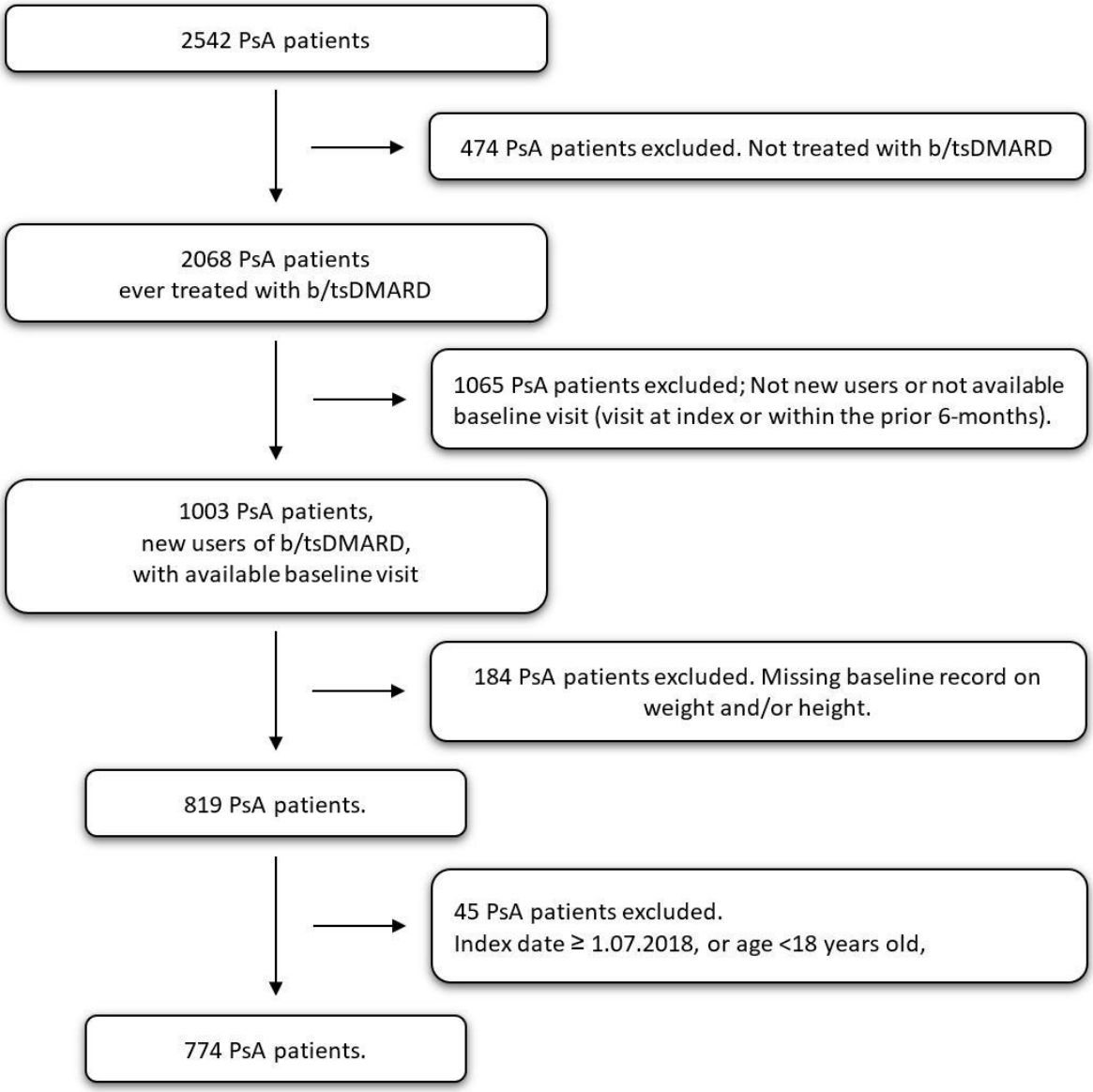
Supplementary Figure S2. Graphical representation of the missingness among baseline variables included in the imputations for primary analysis (i.e., achievement of Minimal Disease Activity (MDA) within the first year after index date). The 48.32% of patients had complete information on all the included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



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

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.

	n sample size	Maximum follow-up 9-months		Maximum follow-up 12-months		Maximum follow-up 15-months	
		n events	ORadj[c] (95% CI)	n events	ORadj[c] (95% CI)	n events	ORadj[c] (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[c]: 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 follow-up 12-months, sensitivity analysis				
	n sample size	n events	OR[a] (95% CI)	Oradj[b] (95% CI)	Oradj[c] (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[c]: 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

Supplementary Table S4. Sensitivity analyses, excluding the 12 patients with body mass index (BMI) <18.5 kg/m^2. 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 (Excluding BMI<18.5)	n sample size	Maximum follow-up 12-months		
		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.

Achieved outcomes								
MDA	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
√	-	√	-	-	4	2	2	0
√	-	-	-	√	4	2	0	2
√	-	√	-	√	13	7	5	1
√	-	-	√	-	12	2	8	2
√	-	√	√	-	1	0	1	0
√	-	-	√	√	2	2	0	0
√	-	√	√	√	6	2	3	1
√	√	√	√	-	6	3	2	1
√	√	√	√	√	74	45	18	11
-	-	√	-	-	15	5	6	4
-	-	-	-	√	98	37	43	18
-	-	√	-	√	68	17	33	18
-	-	√	√	-	1	0	0	1
-	-	-	√	√	1	0	1	0
-	-	√	√	√	6	0	6	0
-	√	√	√	√	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.

STROBE Statement

Obesity and the likelihood of achieving Minimal Disease Activity and remission in psoriatic arthritis patients: a cohort study

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2 (Title and abstract)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-9
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	5-6; 9; Supplementary Figure S5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	8-9
		(*d*) If applicable, explain how loss to follow-up was addressed	6-9
		(*e*) Describe any sensitivity analyses	8-9

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Supplementary Figure S5
		(b) Give reasons for non-participation at each stage	Supplementary Figure S5
		(c) Consider use of a flow diagram	Supplementary Figure S5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	NA (see page 7)
Outcome data	15*	Report numbers of outcome events or summary measures over time	Figure 1; Table 2; Figure 2; Figure 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-12; Figure 1; Table 2
		(*b*) Report category boundaries when continuous variables were categorized	6-7 (exposure and outcome)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-13
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	-
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	-

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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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

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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

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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 PsA patients 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 PsA patients starting their first biologic or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) from 1997 to 30.06.2018. 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 one-year, in overweight and obese patients compared to 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, 285 (36.8%) overweight, and 183 (23.6%) obese patients. Compared to the normal weight group, obese patients had lower odds of achieving MDA at ≤12-months (Adjusted odds ratio [ORadj] 0.45, 95% confidence interval [CI] 0.24-0.82). This was consistent with the observed reduced odds of achieving DAPSA-remission (ORadj 0.42, 95%CI 0.21-0.85), cDAPSA-remission (ORadj 0.51, 95%CI 0.27-0.96), and DAS28-remission (ORadj 0.51, 95%CI 0.32-0.81) in obese vs 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 PsA patients with b/tsDMARDs compared to 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 (SCQM) is a nationwide rheumatology registry that represents one of the largest cohorts of patients with rheumatic diseases, including psoriatic arthritis (PsA).

► 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 (MDA) and remission according to Disease Activity for Psoriatic Arthritis (DAPSA), clinical DAPSA (cDAPSA), and 28-joint Disease Activity Score (DAS28), 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 (e.g., 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 immune-mediated rheumatic disease,[1] with an estimated prevalence of 0.05-0.42%,[2–4] and 5-41% among patients with psoriasis.[3] PsA is a complex and multifactorial disease,[5] 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.[6] Pharmacological treatments include conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) and biologic or targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs).[3] Treatment of PsA aims to maximise health-related quality of life (QoL), through targeting symptoms and structural damage,[7] and it is recommended to target low/minimal disease activity or remission.[6]

One of the most common comorbidities in PsA patients is obesity,[1,8] and higher prevalence of obesity has been reported among PsA patients (23%-37%) compared to the general population.[9–12] Among PsA patients, obesity has been associated to lower probability of achieving Minimal Disease Activity (MDA) compared to patients with normal weight.[10,13,14] Similarly, obese PsA patients treated with tumour necrosis factor alfa inhibitors (TNFi) showed higher risk of treatment discontinuation compared to non-obese patients,[15] as well as lower odds of achieving treatment response compared to non-obese[15] or normal weight patients.[16]

The rationale behind the association between obesity and PsA has been previously discussed.[5,17,18] In short, obesity has been described as a low-grade inflammatory disease,[18] and both obesity and PsA share pathological inflammatory pathways.[5,18,19] 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.[20] Additionally, obesity is a well-known contributor to the metabolic syndrome (MetS), and MetS was similarly associated to lower likelihood of achieving MDA in PsA patients.[21]

Despite the growing evidence on the association between obesity and worse clinical response in PsA patients, 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 PsA patients, but six of the included observational cohorts had a sample size ≤330.[16] 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 BMI in the achievement of MDA and remission in PsA patients. 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 January 1st 1997 and July 31st 2019. The SCQM is a national longitudinal population-based cohort of rheumatic diseases in Switzerland, initiated in 1997.[22] SCQM data are recorded during routine clinical practice, and includes information on demographics, body height and weight, life-style habits, anti-rheumatic medication (with start and stop dates), clinical endpoints, patient-reported outcomes, and health standardized surveys.[12,22] Diagnosis of PsA is recorded in SCQM following the physician's criteria.

Study population

PsA patients (≥18 years old) starting their first b/tsDMARD in the SCQM registry between June 1st 2020 and June 30th 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/m^2) was calculated using height and weight records (**Supplementary 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), overweight (BMI 25.0-29.9), and obese (BMI ≥30). 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) ≤1; number of swollen joint counts (SJC) ≤1; skin manifestation none or almost none; patient's joint pain by visual analogue scale (VAS, 0-100) ≤15; patient's assessment on PsA activity by VAS ≤20; Health Assessment Questionnaire (HAQ) ≤0.5; enthesis points ≤1.[23]

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 **Supplementary 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 one-month between treatment courses of the same b/tsDMARD, as illustrated in the **Supplementary Figure S1**.

Patients with missing information on the study outcomes during the follow-up were categorized 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, anti-rheumatic medication (i.e., b/tsDMARD, csDMARD, corticosteroid), inflammatory markers or acute phase reactants (i.e., ESR, CRP), physician's assessment on disease activity and skin, patient-reported disease activity and pain, tender and swollen joint counts (counting 28 joints), composite disease activity scores (i.e., DAPSA, cDAPSA, DAS28-ESR), disease-specific manifestations (i.e., musculoskeletal manifestations, dactylitis, enthesitis, sacroilitis, spinal involvement, coxitis, peripheral arthritis, nail manifestation), health standardized surveys (i.e., Health Assessment Questionnaire [HAQ], Short Form-12 [SF-12]), and comorbidities (i.e., 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 look-back window, except for: composite disease activity scores, disease-specific

manifestations, and health standardised surveys, which were collected with a 3-months look-back window; Information on smoking, cardiovascular event/disease, and diabetes, which was included if ever reported prior or at index date; And anti-rheumatic medication, which was collected on the index date.

Additional information on covariates is included in Supplementary Text S1.

Data analysis

Patient baseline characteristics were described, and the overweight and obese categories were compared to the normal weight group (reference group) using chi-squared test for categorical variables and t-test, ANOVA, 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[24] in the R Statistical Software.[25] 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 **Supplementary Table S1**. The 48.32% of the study population had complete information on every variable included in the MICE for the main analysis (**Supplementary Figure S2**). Convergence of imputations was assessed by visual inspection of density plots (**Supplementary 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 (DAGs) (**Supplementary 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 standardized 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 one-year outcomes after excluding patients with underweight (BMI<18.5 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 or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

RESULTS

The study included 774 adult PsA patients starting their first b/tsDMARD. **Supplementary 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 to the normal weight group, overweight patients had higher SJC, were less frequently women, and had older mean age. Both overweight and obese patients had lower frequency of high education, and higher patient-reported disease activity and joint pain, while only obese patients had higher CRP levels. Compared to the normal 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 (SF-12pcs) were worse in the obese patients, and patients with obesity were more likely to have had a cardiovascular event/disease than the normal weight group.

214

215 **Table 1.** Patient characteristics at start of first biologic or targeted synthetic disease-modifying

216 anti-rheumatic 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[a]	279 (91.18)	262 (91.93)		160 (87.43)	
other biologic[b]	9 (2.94)	9 (3.16)		6 (3.28)	
tsDMARD[c]	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/h) (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 (26.8)	57 (20)		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 (76.5)	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
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 (8.2)	0.11
Peripheral arthritis	141 (46.08)	138 (48.42)	0.63	94 (51.37)	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)	0.01	26.56 (14.18)	0.07
missing	118 (38.56)	103 (36.14)		77 (42.08)	
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
missing	51 (16.67)	49 (17.19)		34 (18.58)	
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)	

SF-12 pcs (mean (SD))	38.95 (10.67)	37.63 (9.71)	0.18	35.79 (9.04)	0.01
missing	77 (25.16)	78 (27.37)		51 (27.87)	
HAQ (mean (SD))	0.71 (0.66)	0.79 (0.58)	0.20	0.93 (0.61)	0.00
missing	60 (19.61)	59 (20.70)		48 (26.23)	
Cardiovascular event/disease	26 (8.50)	39 (13.68)	0.06	31 (16.94)	0.01
Diabetes or other metabolic problems	10 (3.27)	20 (7.02)	0.06	14 (7.65)	0.05
Depression/anxiety	13 (4.25)	17 (5.96)	0.45	10 (5.46)	0.69

Values are the number and column percentage, unless otherwise specified. Significance tests compare overweight or obese categories to the normal weight group (reference) using chi-squared test for categorical variables, and t-test or ANOVA 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/m^2); Overweight (BMI 25.0-29.9 kg/m^2); Obese (BMI≥30 kg/m^2).

[a] adalimumab, etanercept, infliximab, certolizumab, golimumab; [b] abatacept, secukinumab, tocilizumab, ustekinumab; [c] apremilast.

Abbreviations: BMI body mass index; p p-value; n sample size; SD Standard deviation; IQR Interquartile range; b/tsDMARD biologic or targeted synthetic disease-modifying anti-rheumatic drug; TNFi tumor necrosis factor alpha inhibitor; tsDMARD targeted synthetic disease modifying anti-rheumatic drug; csDMARD conventional synthetic disease modifying anti-rheumatic drug; HLA-B27+ human leukocyte antigen B27 positive; ESR erythrocyte sedimentation rate; mm/h millimetres per hour; CRP C-reactive protein; mg/dL milligrams per decilitre; PsA psoriasis arthritis; DAPSA Disease Activity Index for Psoriatic Arthritis; DAS28 28-joint disease activity score; SF-12 Short-Form 12 health survey (SF-12); mcs mental component summary; pcs physical component summary; HAQ Health Assessment Questionnaire.

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

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-months analyses, the associations of obesity with DAPSA-remission and with cDAPSA-remission were no longer significant (**Table 2**).

Table 2. 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.

	n sample size	Maximum follow-up 9-months			Maximum follow-up 15-months		
		n vents	OR	ORadj	n events	OR	ORadj
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)	0.81 (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)	0.75 (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)
Obese	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)
Obese	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							
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)

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.

In the sensitivity analysis in which the respective composite disease activity score or health standardized 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 (**Supplementary Table S2**). The sensitivity analysis excluding patients with missing information on outcome during the one-year follow-up yielded stronger reduced odds of achieving MDA and remission among abnormal BMI categories vs the normal weight group (**Supplementary Table S3**). The sensitivity analysis excluding the 12 patients with BMI<18.5 yielded similar results to the main study findings **(Supplementary 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 obese, respectively.

The overlap of patients achieving the outcomes during the first year is illustrated in **Figure 3**, complemented with numerical values in **Supplementary Table S5**. Among the 125 patients achieving MDA (66 normal weight, 40 overweight, 19 obese), 80 also achieved DAPSA-remission, of which 48 (72.73%) were normal weight, 20 (50.00%) were overweight, and 12 (63.16%) were obese. Similarly, among patient with MDA, 54 (81.82%) normal weight, 32 (80.00%) overweight, and 15 (78.95%) obese patients 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%) obese patients.

DISCUSSION

This observational cohort study found that obese patients had a significant 49% to 58% reduced odds of achieving MDA, DAPSA-remission, cDAPSA-remission, and DAS28-remission within the first year, when compared to normal weight patients. Conversely, being overweight was only associated with a reduced odds of achieving DAPSA remission. In both high BMI categories, the association with achievement of DAPSA-remLDA within the first year and with one-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 to patients with BMI<30 (hazard ratio 4.90, 95%CI 3.04–7.87).[13] Eder et al. reported that, compared to normal weight patients (BMI<25), overweight and obese patients had 34% and 47% significantly reduced odds of achieving MDA, respectively.[10] While we identified a similar OR in the overweight and obese patients, 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 (EULAR) 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.[26] 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 to non-obese patients (BMI<30), obese patients were associated with a 60% higher risk of TNFi discontinuation during their study period (median follow-up of 1.5 years).[15] 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.[27] Additionally, McGagh and Coates suggested that the 66/68 joint counts provides a more realistic picture of joint involvement in PsA, compared to the 28 joint counts, and highlighted the benefits of including patient-reported outcomes.[28] 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 associate with elevated CRP in the general population.[29–31] This is further supported by the high overlap of patients achieving MDA and cDAPSA-remission in our study, which was similar across every BMI group.

Regarding the observed higher frequency of achievement of DAS28-remission compared to other remission endpoints, 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 obese patients 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 psoriatic arthritis 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.

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

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[37] and the choice of the optimal measure remains challenging.[28] 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 (e.g., dactylitis) and this remains of interest for future studies. Additionally, while standard MDA definition includes Psoriasis Activity and Severity Index (PASI) ≤1 or body surface area (BSA) ≤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, in 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-months 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,[39,40] 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 as normal weight, including patients with BMI<18.5, who may be classified as underweight. This was done due to low prevalence of underweight PsA patients in SCQM[12] and is consistent with previous practice in PsA[10,26] and other inflammatory rheumatic diseases research in which the majority of studies combine normal and underweight patients.[41]

It was suggested that obese patients may benefit from other non-TNFi b/tsDMARDs, however, the evidence is limited.[42] 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 and obese patients was identified as a predictor of MDA achievement,[20] it remains of interest to perform a similar study to this one but stratifying the overweight and obese patients by those with and without weight loss.

CONCLUSION

This study suggests that obesity in PsA patients 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 to 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.

Author Contributions

E.V.-Y., T.B., and A.M.B. contributed to the study conceptualization and methodology; E.V.-Y. performed data curation, formal analysis, visualization, and investigation; E.V.-Y. wrote the original draft manuscript, and T.B., R.M., and A.M.B. contributed with revision and editing. All authors read and agreed to the published version of the manuscript.

Funding

Not applicable. This research received no external funding.

Conflict of interests

None declared.

Ethics approval

This study was reviewed by the ethics commission of the Canton of Zurich (KEK: Req-2020-00045). Pseudonymized 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 authorization.

Patient consent for publication

Not required. Prior enrolment at SCQM, signed Informed Consent is provided by the patients, in accordance with the Declaration of Helsinki. Additionally, withdrawal of participation is possible at any time. Additional patient consent for publication is not required.

Data Availability Statement

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

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FIGURE LEGENDS

(Attached as JPG)

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

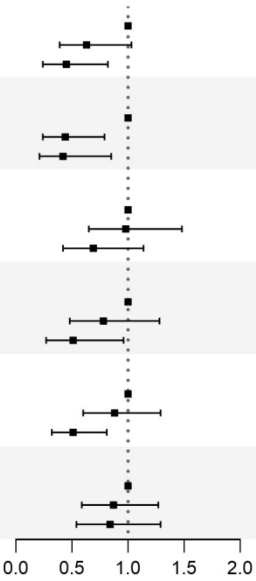
(Attached as JPG)

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 (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSAremLDA DAPSA remission or low disease activity; cDAPSArem clinical DAPSA remission; DAS28rem 28-joint disease activity score remission.

(Attached as JPG)

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 (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSAremLDA DAPSA remission or low disease activity; cDAPSArem clinical DAPSA remission; DAS28rem 28-joint disease activity score remission.

Outcome at ≤12 months unless otherwise specified	sample size, n	n (%) events	OR (95% CI)	ORadj (95% CI)
MDA				
Normal weight	306	66 (21.6)	1 (ref.)	1 (ref.)
Overweight	285	40 (14.0)	0.59 (0.38-0.91)	0.63 (0.39-1.03)
Obese	183	19 (10.4)	0.43 (0.25-0.74)	0.45 (0.24-0.82)
DAPSA-remission				
Normal weight	306	51 (16.7)	1 (ref.)	1 (ref.)
Overweight	285	20 (7.0)	0.38 (0.22-0.66)	0.44 (0.24-0.79)
Obese	183	12 (6.6)	0.36 (0.19-0.70)	0.42 (0.21-0.85)
DAPSA-remLDA				
Normal weight	306	84 (27.5)	1 (ref.)	1 (ref.)
Overweight	285	76 (26.7)	0.95 (0.65-1.37)	0.98 (0.65-1.48)
Obese	183	37 (20.2)	0.67 (0.43-1.04)	0.69 (0.42-1.14)
cDAPSA-remission				
Normal weight	306	57 (18.6)	1 (ref.)	1 (ref.)
Overweight	285	39 (13.7)	0.69 (0.44-1.08)	0.78 (0.48-1.28)
Obese	183	16 (8.7)	0.43 (0.24-0.77)	0.51 (0.27-0.96)
DAS28-remission				
Normal weight	306	115 (37.6)	1 (ref.)	1 (ref.)
Overweight	285	109 (38.2)	0.99 (0.70-1.39)	0.88 (0.6-1.29)
Obese	183	51 (27.9)	0.64 (0.43-0.96)	0.51 (0.32-0.81)
Treatment persistence at the end of month-12				
Normal weight	306	183 (59.8)	1 (ref.)	1 (ref.)
Overweight	285	161 (56.5)	0.84 (0.60-1.17)	0.87 (0.59-1.27)
Obese	183	94 (51.4)	0.71 (0.49-1.03)	0.84 (0.54-1.29)



OR: odds ratio adjusting for: sex, age;

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

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.

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

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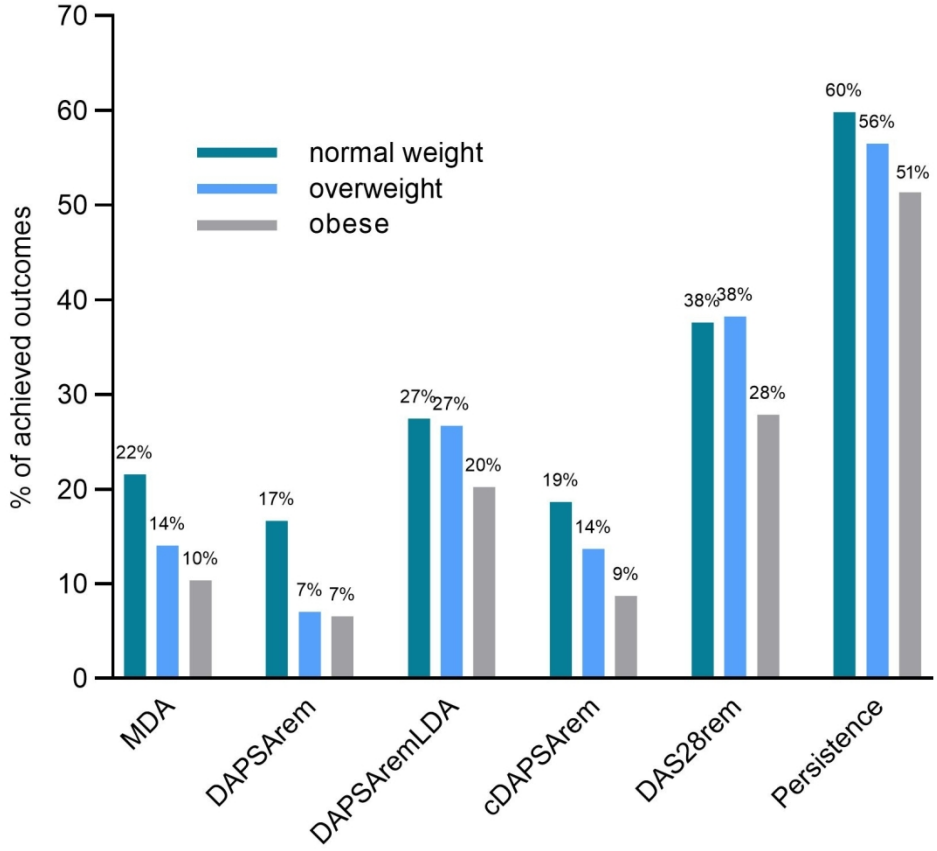

Figure 2. Distribution of patients achieving the study primary and secondary outcomes within the first year, and percentage of patients achieving treatment persistence at the end of month-12, stratified by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity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

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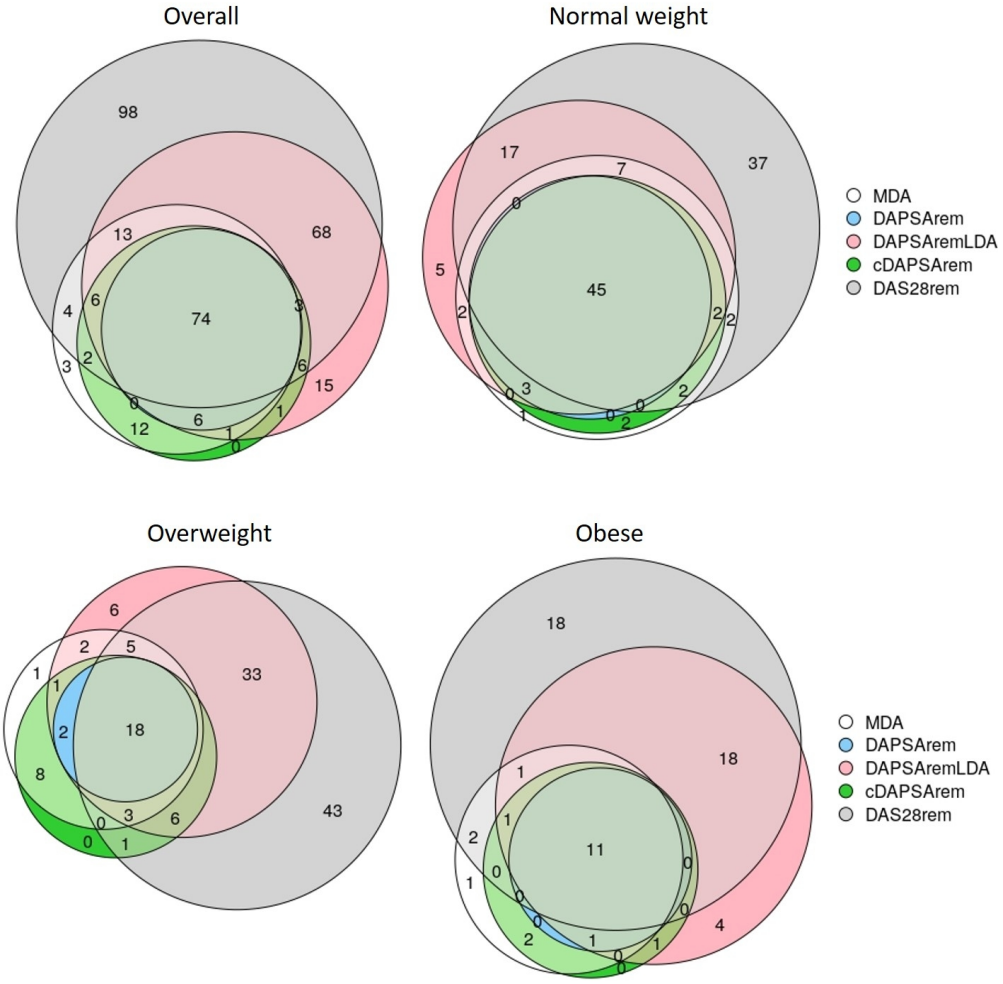

Figure 3. Venn Diagram depicting the number of patients (counts) achieving the study individual primary and secondary outcomes within the first year, overall and stratifying by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis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

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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

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Supplementary Equations

(1) $BMI = \frac{weight\ Kg}{height\ m^2}$

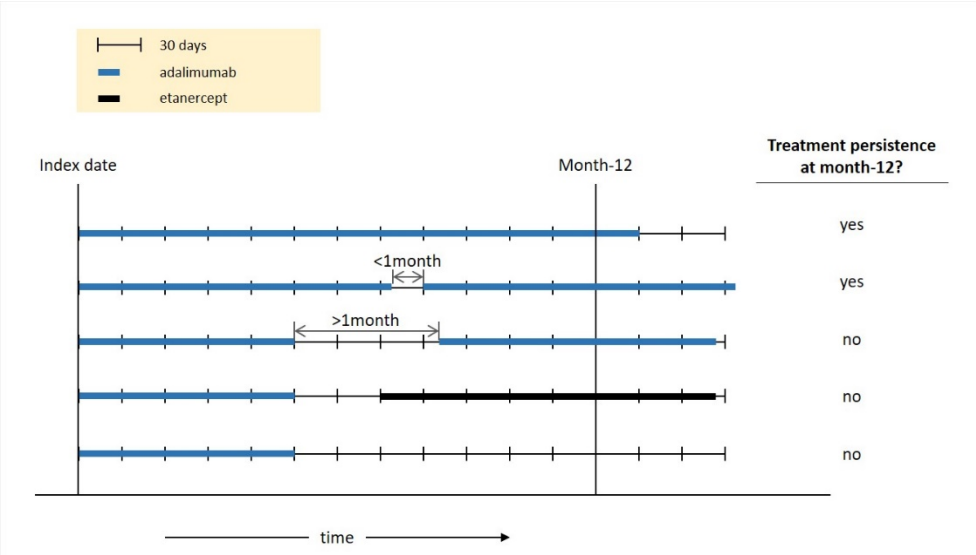
(2) $DAPSA = sjc66 + tjc68 + PatActivity + PatPain + CRP$

(3) $cDAPSA = sjc66 + tjc68 + PatActivity + PatPain$

(4) $DAS28ESR = \left(0.56 \times \sqrt{tjc28}\ + 0.28 \times \sqrt{sjc28}\ + 0.7 \times ln(ESR)\right) \times 1.08 + 0.16$

(5) $DAS28CRP = \left(0.56 \times \sqrt{tjc28}\ + 0.28 \times \sqrt{sjc28}\ + 0.36 \times ln(CRP + 1)\right) \times 1.10 + 1.15$

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).

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.

Supplementary Table S1. Variables included in the multiple imputation.

Variable	Version 1 Included	Version 2 Included	Predicted	Predictor	Method	Missingness	Levels	Range
Outcome[a] (MDA/DAPSArem/DAPSAremLDA/Persistence)	yes	-	-	yes	-	-	yes; no.	-
Outcome[a] (DAS28rem)	-	yes	-	yes	-	-	yes; no.	-
Patient ID	yes	yes	-	-	-	-	-	1-774
BMI category	yes	yes	-	-	-	-	normal weight; overweight; obese.	-
BMI kg/m^2	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 (0-10) (PatActv)	yes	yes	yes	yes	pmm	185 (23.90)	-	0 - 10
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[b]	passive imputation[d]	298 (38.5)	-	0.10 - 121
DAS28	-	yes	yes	yes[c]	passive imputation[e]	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.

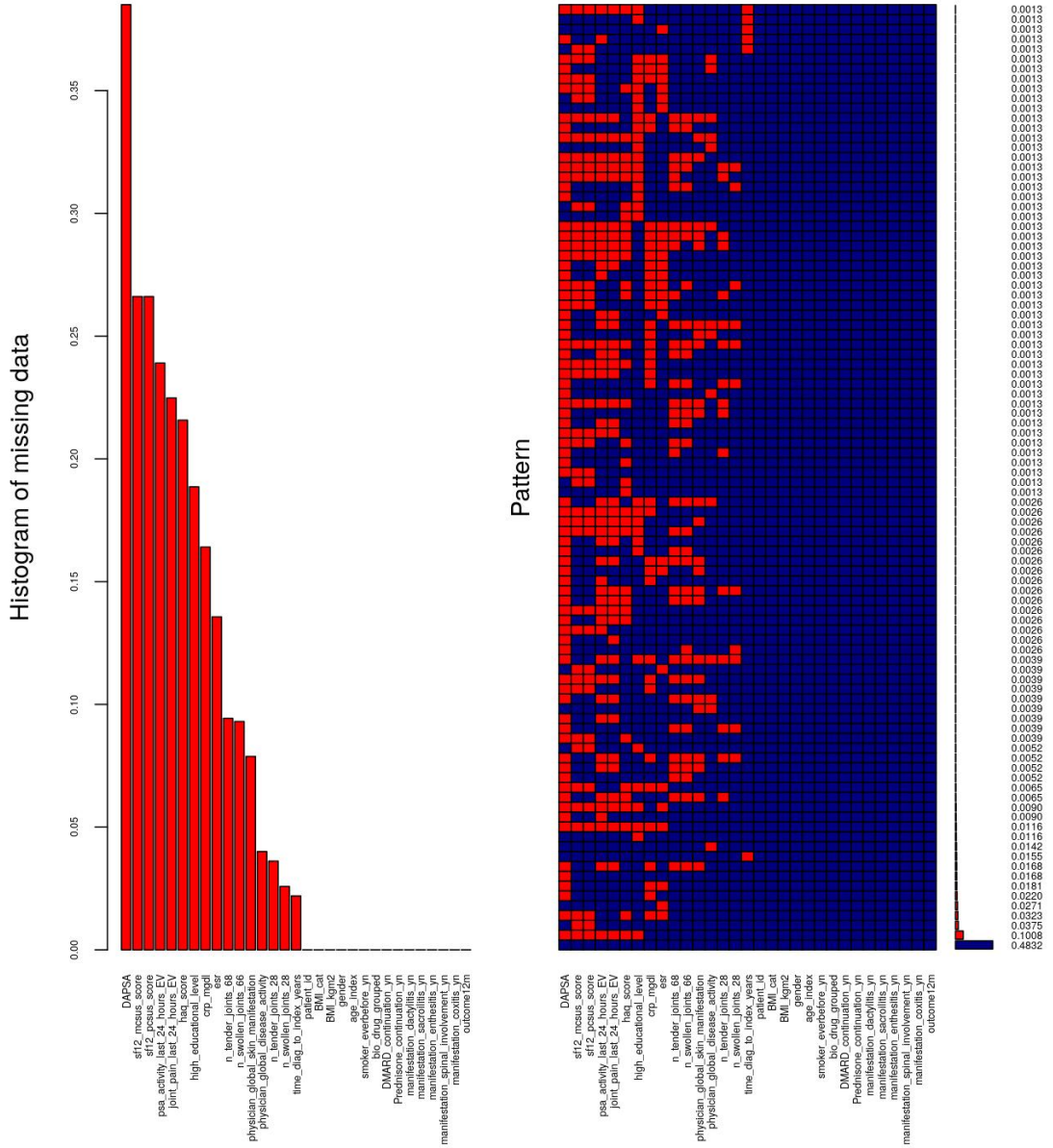
[a] Multiple imputation was run distinctly for each outcome.

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

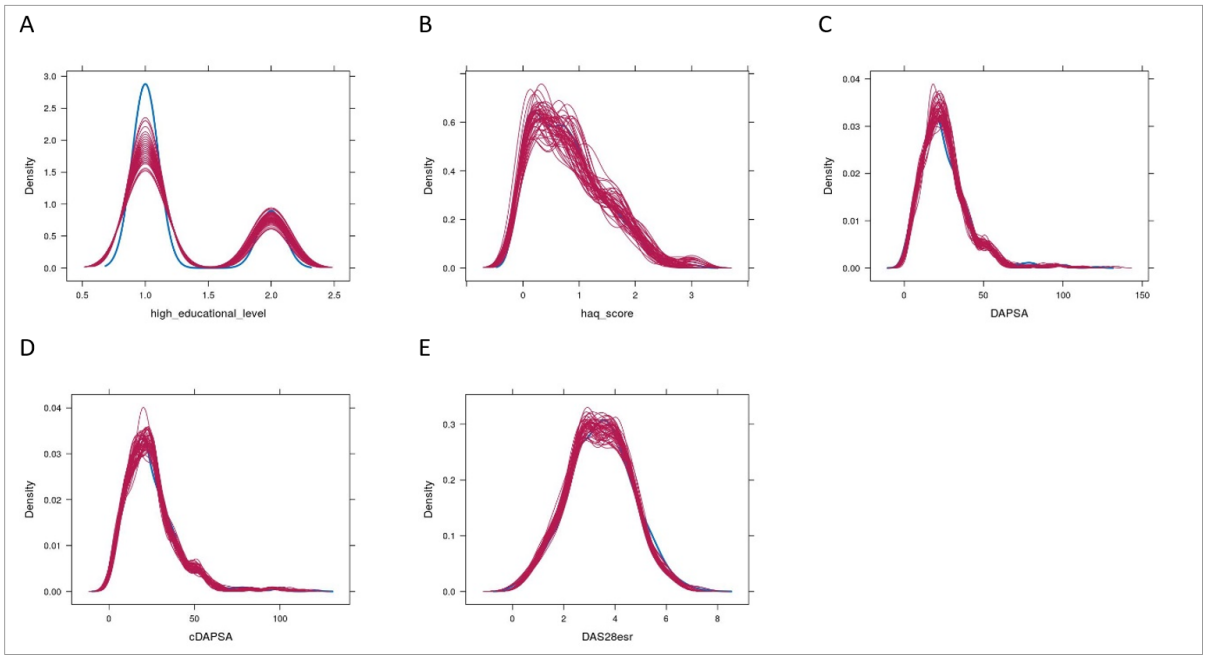
[d] DAS28 not used as predictor for: sjc28, tjc28, ESR.

[d] DAPSA passive imputation: $DAPSA = sjc66 + tjc68 + PatActivity + PatPain + CRP$

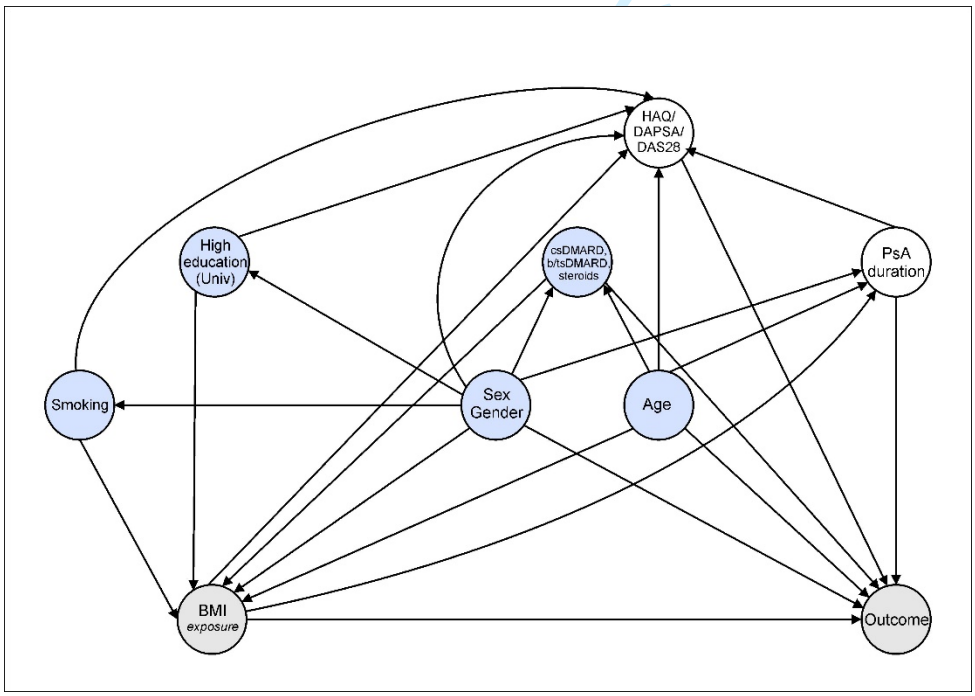
[e] DAS28 passive imputation: $DAS28ESR = \left(0.56 \times \sqrt{tjc28} + 0.28 \times \sqrt{sjc28} + 0.7 \times ln(ESR)\right) \times 1.08 + 0.16$



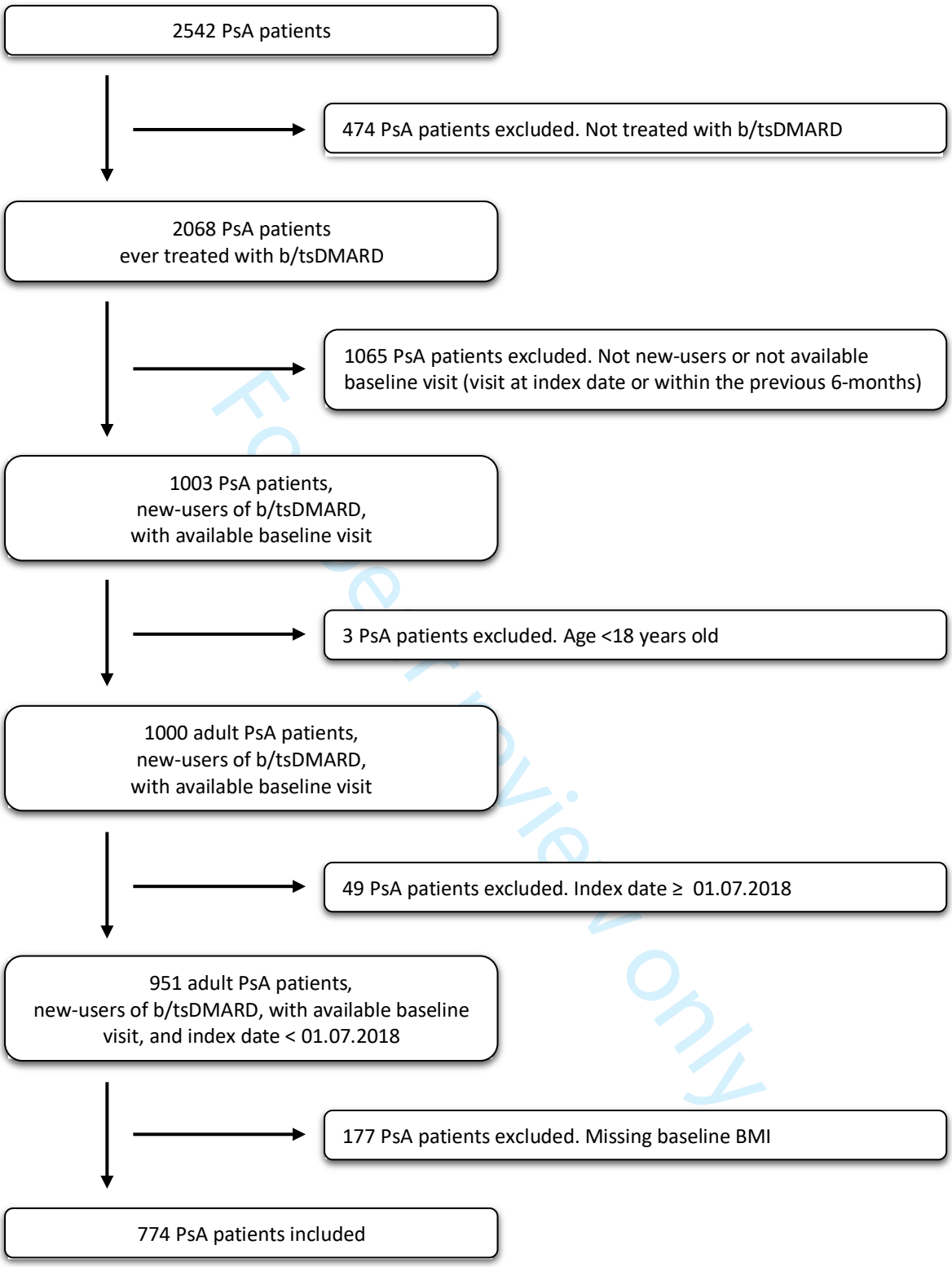
Supplementary Figure S2. Graphical representation of the missingness among baseline variables included in the imputations for primary analysis (i.e., achievement of Minimal Disease Activity (MDA) within the first year after index date). The 48.32% of patients had complete information on all the included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



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

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.

	n sample size	Maximum follow-up 9-months		Maximum follow-up 12-months		Maximum follow-up 15-months	
		n events	ORadj[c] (95% CI)	n events	ORadj[c] (95% CI)	n events	ORadj[c] (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[c]: 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 follow-up 12-months, sensitivity analysis				
	n sample size	n events	OR[a] (95% CI)	Oradj[b] (95% CI)	Oradj[c] (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[c]: 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

Supplementary Table S4. Sensitivity analyses, excluding the 12 patients with body mass index (BMI) <18.5 kg/m^2. 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 (Excluding BMI<18.5)	n sample size	Maximum follow-up 12-months		
		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.

Achieved outcomes								
MDA	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
√	-	√	-	-	4	2	2	0
√	-	-	-	√	4	2	0	2
√	-	√	-	√	13	7	5	1
√	-	-	√	-	12	2	8	2
√	-	√	√	-	1	0	1	0
√	-	-	√	√	2	2	0	0
√	-	√	√	√	6	2	3	1
√	√	√	√	-	6	3	2	1
√	√	√	√	√	74	45	18	11
-	-	√	-	-	15	5	6	4
-	-	-	-	√	98	37	43	18
-	-	√	-	√	68	17	33	18
-	-	√	√	-	1	0	0	1
-	-	-	√	√	1	0	1	0
-	-	√	√	√	6	0	6	0
-	√	√	√	√	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.

STROBE Statement

Obesity and the likelihood of achieving Minimal Disease Activity and remission in psoriatic arthritis patients: a cohort study

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STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2 (Title and abstract)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5-6
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	5-9
Bias	9	Describe any efforts to address potential sources of bias	8-9
Study size	10	Explain how the study size was arrived at	5-6; 9; Supplementary Figure S5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	8-9
		(*d*) If applicable, explain how loss to follow-up was addressed	6-9
		(*e*) Describe any sensitivity analyses	8-9

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Supplementary Figure S5
		(b) Give reasons for non-participation at each stage	Supplementary Figure S5
		(c) Consider use of a flow diagram	Supplementary Figure S5
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	NA (see page 7)
Outcome data	15*	Report numbers of outcome events or summary measures over time	Figure 1; Table 2; Figure 2; Figure 3
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	11-12; Figure 1; Table 2
		(*b*) Report category boundaries when continuous variables were categorized	6-7 (exposure and outcome)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	12-13
Discussion			
Key results	18	Summarise key results with reference to study objectives	13
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	16-17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13-17
Generalisability	21	Discuss the generalisability (external validity) of the study results	-
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	-

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.