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|-------------------------------|--|
| Journal:                      | <i>BMJ Open</i>  |
| Manuscript ID                 | bmjopen-2022-061474  |
| Article Type:                 | Original research  |
| Date Submitted by the Author: | 26-Jan-2022  |
| Complete List of Authors:     | Vallejo-Yagüe, Enriqueta; ETH Zürich, Institute of Pharmaceutical Sciences<br>Burkard, Theresa; ETH Zürich, D-CHAB, Institute of Pharmaceutical Sciences<br>Burden, Andrea; ETH Zurich, Institute of Pharmaceutical Sciences |
| Keywords:                     | RHEUMATOLOGY, EPIDEMIOLOGY, Psoriasis < DERMATOLOGY  |
|                               |  |

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

Abstract word count: 277

Table Strengths and limitations of this study: 159

Manuscript word count: 3114

## 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. Secondly, to assess the accordancy 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  $\leq 12$ -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, accordancy 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  $\leq 12$ -months (Adjusted odds ratio [OR<sub>adj</sub>] 0.45, 95% confidence interval [CI] 0.24-0.82). This was consistent with the observed reduced odds of achieving DAPSA-remission (OR<sub>adj</sub> 0.42, 95%CI 0.21-0.85), cDAPSA-remission (OR<sub>adj</sub> 0.51, 95%CI 0.27-0.96), and DAS28-remission (OR<sub>adj</sub> 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., dactylitis).
- ▶ The study included sensitivity analyses to investigate methodological assumptions.

## INTRODUCTION

Psoriatic arthritis (PsA) is an immune-mediated rheumatic disease,<sup>1</sup> with an estimated prevalence of 0.05-0.42%,<sup>2-4</sup> and 5-41% among patients with psoriasis.<sup>3</sup> PsA is a complex and multifactorial disease,<sup>5</sup> for which pathological features include musculoskeletal involvement, such as inflammation of the peripheral joints (arthritis), the entheses (enthesitis), the axial skeleton (spondylitis), and the finger and toe digits (dactylitis), as well as extra-articular manifestations involving skin and nails, and potentially other organs.<sup>6</sup> Pharmacological treatments include conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs) and biologic or targeted synthetic disease-modifying anti-rheumatic drugs (b/tsDMARDs).<sup>3</sup> Treatment of PsA aims to maximise health-related quality of life (QoL), through targeting symptoms and structural damage,<sup>7</sup> and it is recommended to target low/minimal disease activity or remission.<sup>6</sup>

One of the most common comorbidities in PsA patients is obesity,<sup>1,8</sup> and higher prevalence of obesity has been reported among PsA patients (23%-37%) compared to the general population.<sup>9-12</sup> Among PsA patients, obesity has been associated to lower probability of achieving Minimal Disease Activity (MDA) compared to patients with normal weight.<sup>10,13,14</sup> Similarly, obese PsA patients treated with tumour necrosis factor alfa inhibitors (TNFi) showed higher risk of treatment discontinuation compared to non-obese patients,<sup>15</sup> as well as lower odds of achieving treatment response compared to non-obese<sup>15</sup> or normal weight patients.<sup>16</sup> However, Iannone et al. found no statistically significant differences in remission rates among obese and normal weight PsA patients treated with TNFis.<sup>17</sup> 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.<sup>5,18,19</sup> In short, obesity has been described as a low-grade inflammatory disease,<sup>19</sup> and both obesity and PsA share pathological inflammatory pathways.<sup>5,19,20</sup> Further evidence

1  
2 supporting the association between obesity and a worse PsA clinical outcome is the association  
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4 of weight loss with higher rate of achieving MDA.<sup>21</sup> Additionally, obesity is a well-known  
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6 contributor to the metabolic syndrome (MetS), and MetS was similarly associated to lower  
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8 likelihood of achieving MDA in PsA patients.<sup>22</sup>  
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10  
11 These findings support the need to study PsA patients with elevated BMI. Thus, we seek  
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13 to contribute to the growing body of evidence by performing an observational cohort study  
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15 aiming to assess the impact of BMI in the achievement of MDA and remission in PsA patients.  
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17 Additionally, by including several outcome definitions we aim to investigate the consistency  
18  
19 of the findings when considering different aspects of the disease.  
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## 22 23 **METHODS**

### 24 25 **Study design and data source**

26  
27 We performed an observational cohort study in the Swiss Clinical Quality Management in  
28  
29 Rheumatic Diseases (SCQM) registry from January 1<sup>st</sup> 1997 and July 31<sup>st</sup> 2019. The SCQM is  
30  
31 a national longitudinal population-based cohort of rheumatic diseases in Switzerland, initiated  
32  
33 in 1997.<sup>23</sup> SCQM data are recorded during routine clinical practice, and includes information  
34  
35 on demographics, body height and weight, life-style habits, anti-rheumatic medication (with  
36  
37 start and stop dates), clinical endpoints, patient-reported outcomes, and fragility and health  
38  
39 standardized surveys.<sup>12,23</sup>  
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### 44 45 **Study population**

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47 PsA patients ( $\geq 18$  years old) starting their first b/tsDMARD in the SCQM registry between  
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49 January 1<sup>st</sup> 1997 and June 30<sup>th</sup> 2018 (inclusive) were included in the study. The first recorded  
50  
51 start of b/tsDMARD in the SCQM was defined as the index date. Patients with a b/tsDMARD  
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53 start date before their first registered visit at SCQM were excluded. Similarly, patients without  
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55 a baseline record on height and weight were excluded.  
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## Exposure

The exposure of interest was BMI category at the start of the patients' first b/tsDMARD. Baseline BMI (kg/m<sup>2</sup>) 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; enthesitis points ≤1.<sup>24</sup>

Secondary outcomes assessed within the first year were: achievement of Disease Activity for Psoriatic Arthritis (DAPSA) remission, defined as DAPSA ≤4; DAPSA remission or low disease activity (DAPSA-remLDA), defined as DAPSA ≤14; clinical DAPSA (cDAPSA) remission, defined as cDAPSA ≤4; and 28-joint disease activity score (DAS28) remission, defined as DAS28 < 2.6. DAPSA, cDAPSA, and DAS28 formulas are described in the **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**.

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2 Patients with missing information on the study outcomes during the follow-up were  
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4 categorized as not having achieved the corresponding outcome. In a sensitivity analysis, we re-  
5  
6 ran our analyses excluding patients with missing information on outcome during follow-up.  
7

### 8 9 **Follow-up**

10 For primary and secondary outcomes, patients were followed from index date until  
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12 achievement of outcome or a maximum follow-up of 12-months. For the tertiary outcome  
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14 (treatment persistence) patients were followed until the earliest of the following: treatment stop,  
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16 start of a new b/tsDMARD, or end of observation period (12-months).  
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19  
20 In a secondary analysis, all outcomes were assessed with a maximum follow-up of 9-  
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22 months and 15-months. This was done to investigate if the findings would differ across shorter  
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24 and longer follow-up times.  
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### 27 28 **Covariates**

29 Baseline variables included demographics, BMI, high education, ever smoking, anti-rheumatic  
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31 medication (i.e., b/tsDMARD, csDMARD, corticosteroid), inflammatory markers, physician's  
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33 assessment on disease activity and skin, patient-reported disease activity and pain, joint counts,  
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35 disease activity scores (i.e., DAPSA, cDAPSA, DAS28-ESR), disease-specific manifestations  
36  
37 (i.e., musculoskeletal manifestations, dactylitis, enthesitis, sacroilitis, spinal involvement,  
38  
39 coxitis, peripheral arthritis, nail manifestation), fragility and health standardized surveys (i.e.,  
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41 Health Assessment Questionnaire [HAQ], Short Form-12 [SF-12]), and comorbidities (i.e.,  
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43 cardiovascular event/disease, diabetes or other metabolic problems, depression/anxiety).  
44  
45 Baseline variables were collected at index date, or as close as possible to that date within a 6-  
46  
47 month look-back window, except for: disease activity scores, disease-specific manifestations,  
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49 and fragility and health surveys, which were collected with a 3-months look-back window.  
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51 Information on smoking, cardiovascular event/disease, and diabetes, which was included if  
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53 ever reported prior or at index date. Anti-rheumatic medication which was collected on the  
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55 index date.  
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## 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<sup>25</sup> in the R Statistical Software.<sup>26</sup> MICE was performed for each study outcome separately, using 50 imputations with 15 interactions for each set. Variables included in the imputations, their original missingness, and corresponding applied imputation models are presented in the **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.

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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<br>(n=306) | Overweight<br>(n=285) | p-value | Obese<br>(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<sup>2</sup>); Overweight (BMI 25.0-29.9 kg/m<sup>2</sup>); Obese (BMI ≥30 kg/m<sup>2</sup>). 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 (OR<sub>adj</sub>) 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 OR<sub>adj</sub> 0.44 [95% CI 0.24-0.79] and obese OR<sub>adj</sub> 0.42 [95% CI 0.21-0.85]), compared to normal weight patients. Additionally, obese patients had reduced odds of achieving cDAPSA-remission (OR<sub>adj</sub> 0.51 [95% CI 0.27-0.96]) and DAS28-remission (OR<sub>adj</sub> 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            |
| <b>MDA</b>   |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>DAPSA-remission</b>                               |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>DAPSA-remLDA</b>                                  |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>cDAPSA-remission</b>                              |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>DAS28-remission</b>                               |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>Treatment persistence at the end of follow-up</b> |                            |                  |                  |                             |                  |                  |
| 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.<sup>10,13,15</sup> 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).<sup>13</sup> Eder et al. reported that, compared to normal weight patients



1  
2 (BMI<25), overweight and obese patients had 34% and 47% significantly reduced odds of  
3  
4 achieving MDA, respectively.<sup>10</sup> While we identified a similar OR in the overweight and obese  
5  
6 patients, our results in the overweight group were not statistically significant. In the study by  
7  
8 Højgaard et al., obesity was associated with 53% lower odds of achieving European Alliance  
9  
10 of Associations for Rheumatology (EULAR) good or moderate (EGOM) response.<sup>15</sup> While we  
11  
12 did not assess EGOM response, this is a DAS28-driven outcome, and the findings are in  
13  
14 agreement with our observed association between obesity and 49% reduced odds for DAS28-  
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16 remission. Conversely, Iannone et al. suggested no significant differences in DAS28-remission  
17  
18 rates across BMI categories.<sup>17</sup> However, they had a small sample size (135 patients), and their  
19  
20 observed lower remission rate in the obese vs normal weight patients was in line with our  
21  
22 findings.  
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26  
27 Additionally, results from Højgaard et al. showed that compared to non-obese patients  
28  
29 (BMI<30), obese patients were associated with a 60% higher risk of TNFi discontinuation  
30  
31 during their study period (median follow-up of 1.5 years).<sup>15</sup> While our study did not yield an  
32  
33 association between BMI and treatment persistence, these contrasting findings may be  
34  
35 explained by the different methodologies. Højgaard et al. assessed the time to withdrawal using  
36  
37 a survival model, which gives high attention to early outcomes, while we investigated  
38  
39 persistence yes/no at a specific timepoint using logistic regression. Clinicians may be inclined  
40  
41 to continue with therapy longer in obese than in normal weight patients, given the higher  
42  
43 disease activity at baseline and knowing that obese patients may be less likely to achieve MDA  
44  
45 or remission. While this could impact the time to treatment stop, it may not affect the  
46  
47 persistence at a relatively advanced time-point.  
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53 In our study MDA was the main outcome as it covers several aspects from the disease  
54  
55 presentation and consequences, and has been associated with patient's QoL and productivity.<sup>27</sup>  
56  
57 Additionally, McGagh and Coates suggested that the 66/68 joint counts provides a more  
58  
59 realistic picture of joint involvement in PsA, compared to the 28 joint counts, and highlighted  
60

1  
2 the benefits of including patient-reported outcomes.<sup>28</sup> Based on this, we identified DAPSA-  
3  
4 remission and cDAPSA-remission as optimal secondary outcomes. However, we expect that  
5  
6 cDAPSA may be a better fit to study patients with abnormal BMI since obesity was associate  
7  
8 with elevated CRP in the general population.<sup>29-31</sup> This is further supported by the high overlap  
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10 of patients achieving MDA and cDAPSA-remission in our study, which was similar across  
11  
12 every BMI group.  
13  
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15  
16 Regarding the observed higher frequency of achievement of DAS28-remission compared  
17  
18 to other remission endpoints, this may be explained by its narrow focus on peripheral  
19  
20 manifestations, potentially underestimating residual disease activity. Nevertheless, the  
21  
22 consistency of the observed results on MDA and remission outcomes in the obese group  
23  
24 suggests that obesity affects peripheral joints, as well as disease-specific manifestations and  
25  
26 the patient's perspective. However, we note that the different outcome definitions led to  
27  
28 contrasting results in the overweight group, suggesting that the effect of overweight on the PsA  
29  
30 may not be fully captured by every remission definition. Similarly, the impact of obesity on  
31  
32 PsA clinical response was not consistent with the more clinically accessible outcome low  
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34 disease activity (DAPSA-remLDA).  
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### 38 **Strengths and limitations**

39  
40 In addition to the large sample size, the key strength of this study is the use of several relevant  
41  
42 clinical outcome definitions. While multiple approaches to assess PsA disease activity exist,  
43  
44 no single one has been identified as sufficient<sup>32</sup> and the choice of the optimal measure remains  
45  
46 challenging.<sup>28</sup> The consistency of the observed results on MDA and remission outcomes in the  
47  
48 obese group reinforces the study findings. However, we did not look at unidimensional  
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50 outcomes (e.g., dactylitis) and this remains of interest for future studies.  
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55 Our results were mainly consistent among various sensitivity analyses. Excluding  
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57 patients missing information on the outcome during follow-up (instead of treating them as non-  
58  
59 achievers of the respective outcome), supported the observed effect of obesity towards MDA  
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1  
2 and remission, which was even accentuated in this sensitivity analysis. Among secondary  
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4 analyses varying the duration of follow-up, the 15-month analyses showed consistence with  
5  
6 the main findings, and the reduced effect found in the 9-months analyses may be explained by  
7  
8 higher missingness of outcome information at shorter follow-up, and therefore lower number  
9  
10 of observed events overall.  
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13  
14 Limitations to consider when interpreting the results include the potential  
15  
16 misclassification of patients in the BMI categories. While overweight and obesity are  
17  
18 commonly defined by BMI,<sup>33,34</sup> this lacks information on body composition. Thus, although  
19  
20 data on waist circumference, skinfold thickness, and bioelectrical impedance may provide a  
21  
22 better patient classification, this information is extremely limited in real-world data.  
23  
24 Additionally, we classified patients with BMI<25 as normal weight, including patients with  
25  
26 BMI<18.5, who may be classified as underweight. This was done due to low prevalence of  
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28 underweight PsA patients in SCQM<sup>12</sup> and is consistent with previous practice in PsA<sup>10,17</sup> and  
29  
30 other inflammatory rheumatic diseases research in which the majority of studies combine  
31  
32 normal and underweight patients.<sup>35</sup>  
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36  
37 Finally, since weight loss in overweight and obese patients was identified as a predictor  
38  
39 of MDA achievement,<sup>21</sup> it remains of interest to perform a similar study to this one but  
40  
41 stratifying the overweight and obese patients by those with and without weight loss.  
42  
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## 45 **CONCLUSION**

46  
47 This study suggests that obesity in PsA patients is associated with at least a 50% reduction in  
48  
49 the likelihood of achieving MDA or remission within the first year after starting b/tsDMARD  
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51 therapy, when compared to normal weight patients. The consistency of findings across  
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53 definitions of remission suggests that obesity affects several factors of PsA disease.  
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55 Conversely, obesity was neither associated with the likelihood of achieving low disease activity  
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57 nor with treatment persistence. Finally, comparative analyses of b/tsDMARDs within BMI  
58  
59  
60

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.

## **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).

## Acknowledgments

We thank all patients and rheumatologists contributing to the SCQM registry, as well as the entire SCQM staff. A list of rheumatology offices and hospitals which contribute to the SCQM registry can be found at <http://www.scqm.ch/institutions>. A list of financial supporters of SCQM can be found at <http://www.scqm.ch/sponsors>. We would like to add a personal thank you to Axel Finckh (University Hospitals of Geneva) for his input regarding the database. AMB acknowledges that her professorship is partly endowed by the Swiss National Pharmacy Association (PharmaSuisse) and the ETH Foundation.

## Supplementary Material

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## REFERENCES

- 1 Kumthekar A, Ogdie A. Obesity and Psoriatic Arthritis: A Narrative Review. *Rheumatol Ther* 2020; **7**: 447–56.
- 2 Salaffi F, De Angelis R, Grassi W, MArche Pain Prevalence, INvestigation Group (MAPPING) study. Prevalence of musculoskeletal conditions in an Italian population sample: results of a regional community-based study. I. The MAPPING study. *Clin Exp Rheumatol* 2005; **23**: 819–28.
- 3 Ogdie A, Weiss P. The Epidemiology Psoriatic Arthritis. *Rheum Dis Clin North Am* 2015; **41**: 545–68.
- 4 Scotti L, Franchi M, Marchesoni A, Corrao G. Prevalence and incidence of psoriatic arthritis: A systematic review and meta-analysis. *Semin Arthritis Rheum* 2018; **48**: 28–34.

- 1  
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3  
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6  
7  
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52  
53  
54  
55  
56  
57  
58  
59  
60
- 5 Porta S, Otero-Losada M, Kölliker Frers RA, Cosentino V, Kerzberg E, Capani F. Adipokines, Cardiovascular Risk, and Therapeutic Management in Obesity and Psoriatic Arthritis. *Front Immunol* 2021; **11**. DOI:10.3389/fimmu.2020.590749.
  - 6 Gossec L, Smolen JS, Ramiro S, *et al*. European League Against Rheumatism (EULAR) recommendations for the management of psoriatic arthritis with pharmacological therapies: 2015 update. *Annals of the Rheumatic Diseases* 2016; **75**: 499–510.
  - 7 Gossec L, Baraliakos X, Kerschbaumer A, *et al*. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. *Annals of the Rheumatic Diseases* 2020; **79**: 700–12.
  - 8 Gupta S, Syrimi Z, Hughes DM, Zhao SS. Comorbidities in psoriatic arthritis: a systematic review and meta-analysis. *Rheumatol Int* 2021; **41**: 275–84.
  - 9 Bhole VM, Choi HK, Burns LC, *et al*. Differences in body mass index among individuals with PsA, psoriasis, RA and the general population. *Rheumatology* 2012; **51**: 552–6.
  - 10 Eder L, Thavaneswaran A, Chandran V, Cook RJ, Gladman DD. Obesity is associated with a lower probability of achieving sustained minimal disease activity state among patients with psoriatic arthritis. *Ann Rheum Dis* 2015; **74**: 813–7.
  - 11 Eder L, Abji F, Rosen CF, Chandran V, Gladman DD. The Association Between Obesity and Clinical Features of Psoriatic Arthritis: A Case-control Study. *J Rheumatol* 2017; **44**: 437–43.
  - 12 Vallejo-Yagüe E, Burkard T, Möller B, Finckh A, Burden AM. Comparison of Psoriatic Arthritis and Rheumatoid Arthritis Patients across Body Mass Index Categories in Switzerland. *Journal of Clinical Medicine* 2021; **10**: 3194.
  - 13 di Minno MND, Peluso R, Iervolino S, *et al*. Obesity and the prediction of minimal disease activity: a prospective study in psoriatic arthritis. *Arthritis Care Res (Hoboken)* 2013; **65**: 141–7.
  - 14 Lupoli R, Pizzicato P, Scalera A, *et al*. Impact of body weight on the achievement of minimal disease activity in patients with rheumatic diseases: a systematic review and meta-analysis. *Arthritis Res Ther* 2016; **18**: 297.
  - 15 Højgaard P, Glinborg B, Kristensen LE, Gudbjornsson B, Love TJ, Dreyer L. The influence of obesity on response to tumour necrosis factor- $\alpha$  inhibitors in psoriatic arthritis: results from the DANBIO and ICEBIO registries. *Rheumatology* 2016; **55**: 2191–9.
  - 16 Singh S, Facciorusso A, Singh AG, *et al*. Obesity and response to anti-tumor necrosis factor- $\alpha$  agents in patients with select immune-mediated inflammatory diseases: A systematic review and meta-analysis. *PLoS One* 2018; **13**: e0195123.
  - 17 Iannone F, Fanizzi R, Scioscia C, Anelli MG, Lapadula G. Body mass does not affect the remission of psoriatic arthritis patients on anti-TNF- $\alpha$  therapy. *Scandinavian Journal of Rheumatology* 2013; **42**: 41–4.
  - 18 Versini M, Jeandel P-Y, Rosenthal E, Shoenfeld Y. Obesity in autoimmune diseases: Not a passive bystander. *Autoimmunity Reviews* 2014; **13**: 981–1000.



- 1  
2 19Russolillo A, Iervolino S, Peluso R, *et al.* Obesity and psoriatic arthritis: from pathogenesis  
3 to clinical outcome and management. *Rheumatology* 2013; **52**: 62–7.  
4  
5 20Neumann E, Hasseli R, Ohl S, Lange U, Frommer KW, Müller-Ladner U. Adipokines and  
6 Autoimmunity in Inflammatory Arthritis. *Cells* 2021; **10**. DOI:10.3390/cells10020216.  
7  
8 21Minno MNDD, Peluso R, Iervolino S, *et al.* Weight loss and achievement of minimal disease  
9 activity in patients with psoriatic arthritis starting treatment with tumour necrosis factor  $\alpha$   
10 blockers. *Annals of the Rheumatic Diseases* 2014; **73**: 1157–62.  
11  
12 22Costa L, Caso F, Ramonda R, *et al.* Metabolic syndrome and its relationship with the  
13 achievement of minimal disease activity state in psoriatic arthritis patients: an observational  
14 study. *Immunol Res* 2015; **61**: 147–53.  
15  
16 23Die SCQM Foundation (Swiss Clinical Quality Management in Rheumatic Diseases).  
17 <https://www.scqm.ch/en/ueber-uns/> (accessed May 18, 2021).  
18  
19 24Coates LC, Strand V, Wilson H, *et al.* Measurement properties of the minimal disease  
20 activity criteria for psoriatic arthritis. *RMD Open* 2019; **5**. DOI:10.1136/rmdopen-2019-  
21 001002.  
22  
23 25Buuren S van, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained  
24 Equations in R. *Journal of Statistical Software* 2011; **45**: 1–67.  
25  
26 26R Core Team (2020). R: A language and environmental for statistical computing. R  
27 Foundation for Statistical Computing, Vienna, Austria. <https://www.r-project.org/>  
28 (accessed May 14, 2021).  
29  
30 27Coates LC, Orbai A-M, Morita A, *et al.* Achieving minimal disease activity in psoriatic  
31 arthritis predicts meaningful improvements in patients' health-related quality of life and  
32 productivity. *BMC Rheumatology* 2018; **2**: 24.  
33  
34 28McGagh D, Coates LC. Assessment of the many faces of PsA: single and composite  
35 measures in PsA clinical trials. *Rheumatology* 2020; **59**: i29–36.  
36  
37 29Yudkin JS, Stehouwer CDA, Emeis JJ, Coppack SW. C-Reactive Protein in Healthy  
38 Subjects: Associations With Obesity, Insulin Resistance, and Endothelial Dysfunction.  
39 *Arteriosclerosis, Thrombosis, and Vascular Biology* 1999; **19**: 972–8.  
40  
41 30Hak AE, Stehouwer CDA, Bots ML, *et al.* Associations of C-Reactive Protein With  
42 Measures of Obesity, Insulin Resistance, and Subclinical Atherosclerosis in Healthy,  
43 Middle-Aged Women. *Arteriosclerosis, Thrombosis, and Vascular Biology* 1999; **19**: 1986–  
44 91.  
45  
46 31Visser M. Elevated C-Reactive Protein Levels in Overweight and Obese Adults. *JAMA*  
47 1999; **282**: 2131.  
48  
49 32Gulfe A, Geborek P, Saxne T. Response criteria for rheumatoid arthritis in clinical practice:  
50 how useful are they? *Ann Rheum Dis* 2005; **64**: 1186–9.  
51  
52 33Body mass index - BMI. [https://www.euro.who.int/en/health-topics/disease-](https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi)  
53 [prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi](https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi) (accessed June 23, 2021).  
54  
55  
56  
57  
58  
59  
60

1  
2 34 Obesity and overweight. [https://www.who.int/news-room/fact-sheets/detail/obesity-and-](https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight)  
3 overweight (accessed July 8, 2021).  
4

5 35 Lee Y, Kwan Y, Lim K, *et al.* A systematic review of the association of obesity with the  
6 outcomes of inflammatory rheumatic diseases. *smedj* 2019; **60**: 270–80.  
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For peer review only



## 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; DAPSRem Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSRemLDA DAPSA remission or low disease activity; cDAPSRem 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; DAPSRem Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSRemLDA DAPSA remission or low disease activity; cDAPSRem clinical DAPSA remission; DAS28rem 28-joint disease activity score remission.

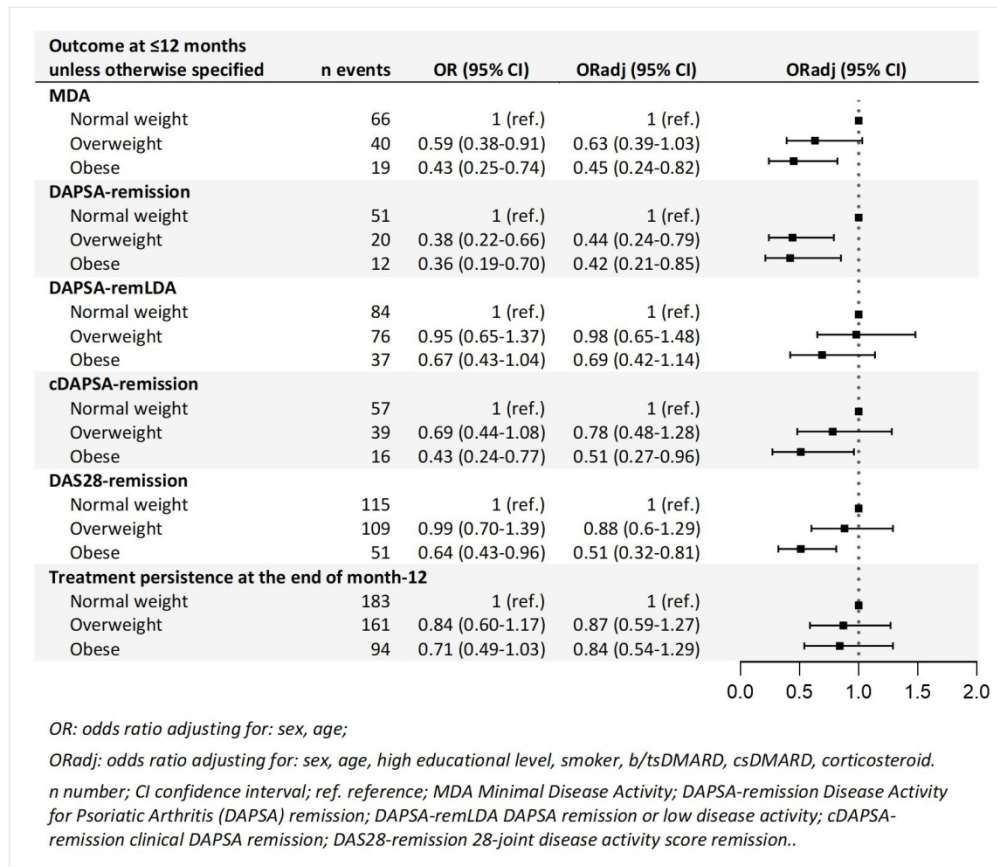


Figure 1. Results from the multivariable logistic regression investigating the association between body mass index (BMI) categories and various clinical outcomes. Maximum follow-up 12-months.

286x248mm (144 x 144 DPI)

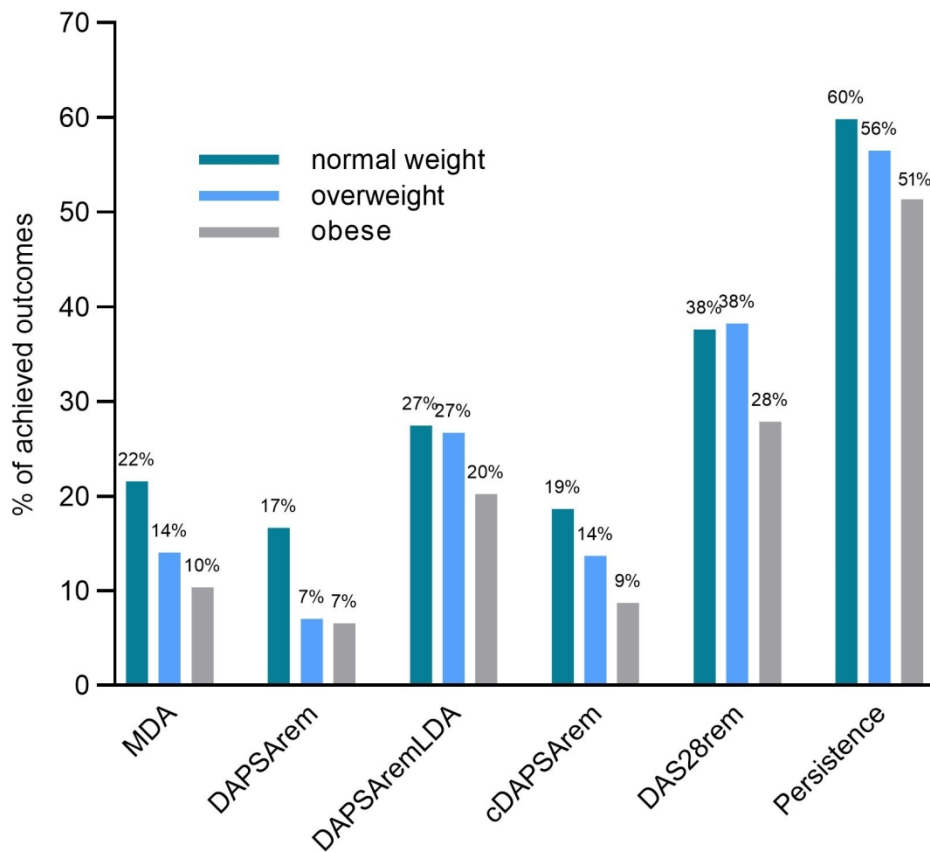


Figure 2. Distribution of patients achieving the study primary and secondary outcomes within the first year, and percentage of patients achieving treatment persistence at the end of month-12, stratified by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity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

306x275mm (144 x 144 DPI)

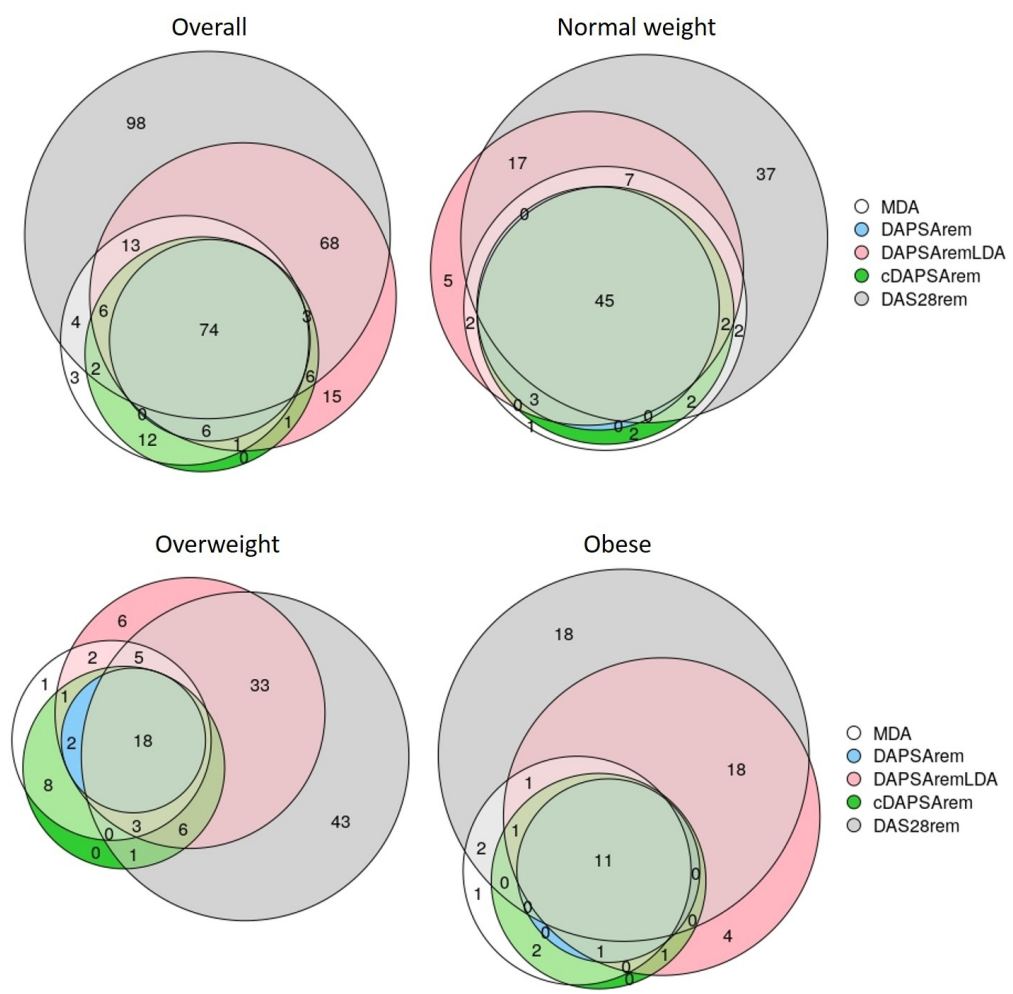


Figure 3. Venn Diagram depicting the number of patients (counts) achieving the study individual primary and secondary outcomes within the first year, overall and stratifying by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis (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

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

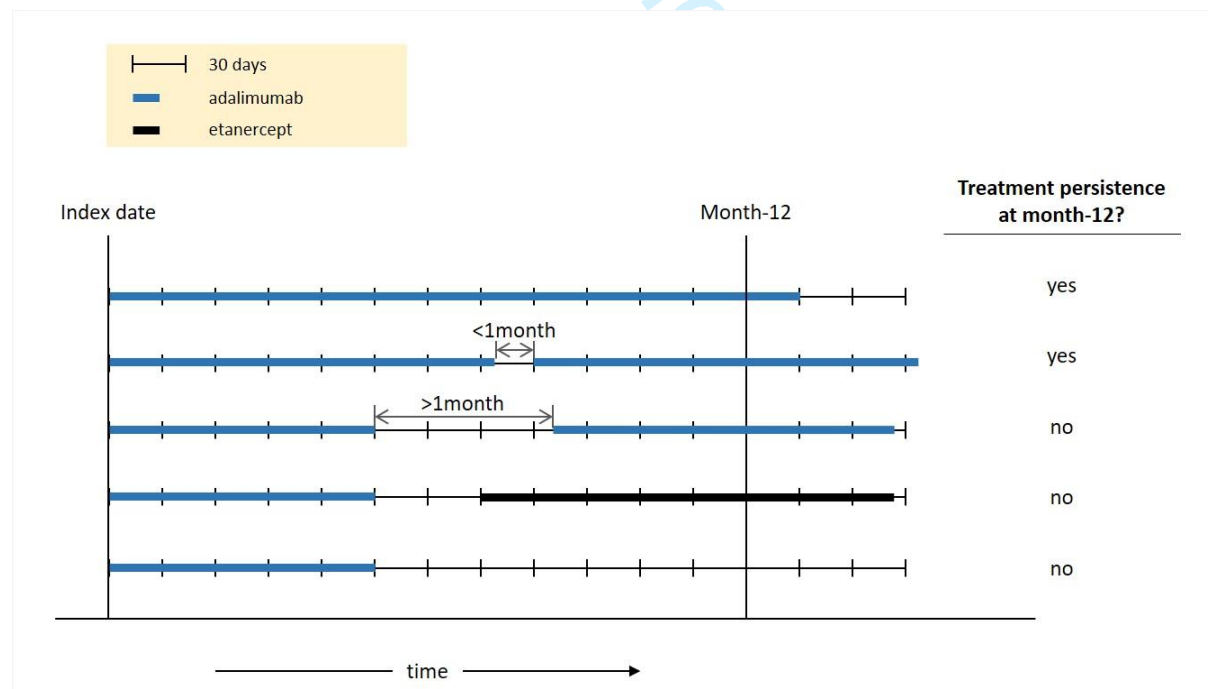
$$(2) \text{ DAPSA} = \text{sjc66} + \text{tjc68} + \text{PatActivity} + \text{PatPain} + \text{CRP}$$

$$(3) \text{ cDAPSA} = \text{sjc66} + \text{tjc68} + \text{PatActivity} + \text{PatPain}$$

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

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

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



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

**Supplementary Table S1.** Variables included in the multiple imputation.

| Variable  | Version 1 Included | Version 2 Included | Predicted | Predictor        | Method                          | Missingness | Levels   | Range         |
|---|--------------------|--------------------|-----------|------------------|---------------------------------|-------------|--|---------------|
| Outcome <sup>a</sup> (MDA/DAPSArem/DAPSAremLDA/Persistence) | yes                | -                  | -         | yes              | -                               | -           | yes; no.   | -             |
| Outcome <sup>a</sup> (DAS28rem)                             | -                  | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Patient ID  | yes                | yes                | -         | -                | -                               | -           | -  | 1-774         |
| BMI category  | yes                | yes                | -         | -                | -                               | -           | normal weight; overweight; obese.  | -             |
| BMI kg/m <sup>2</sup>                                       | 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 <sup>b</sup> | passive imputation <sup>d</sup> | 298 (38.5)  | -  | 0.10 - 121    |
| DAS28   | -                  | yes                | yes       | yes <sup>c</sup> | passive imputation <sup>e</sup> | 99 (12.79)  | -  | 0.20 - 7.60   |
| HAQ (0-3)   | yes                | yes                | yes       | yes              | pmm                             | 167 (21.58) | -  | 0 - 3         |
| SF-12mcs (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.   | -             |
| Sacroiliitis  | 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.

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

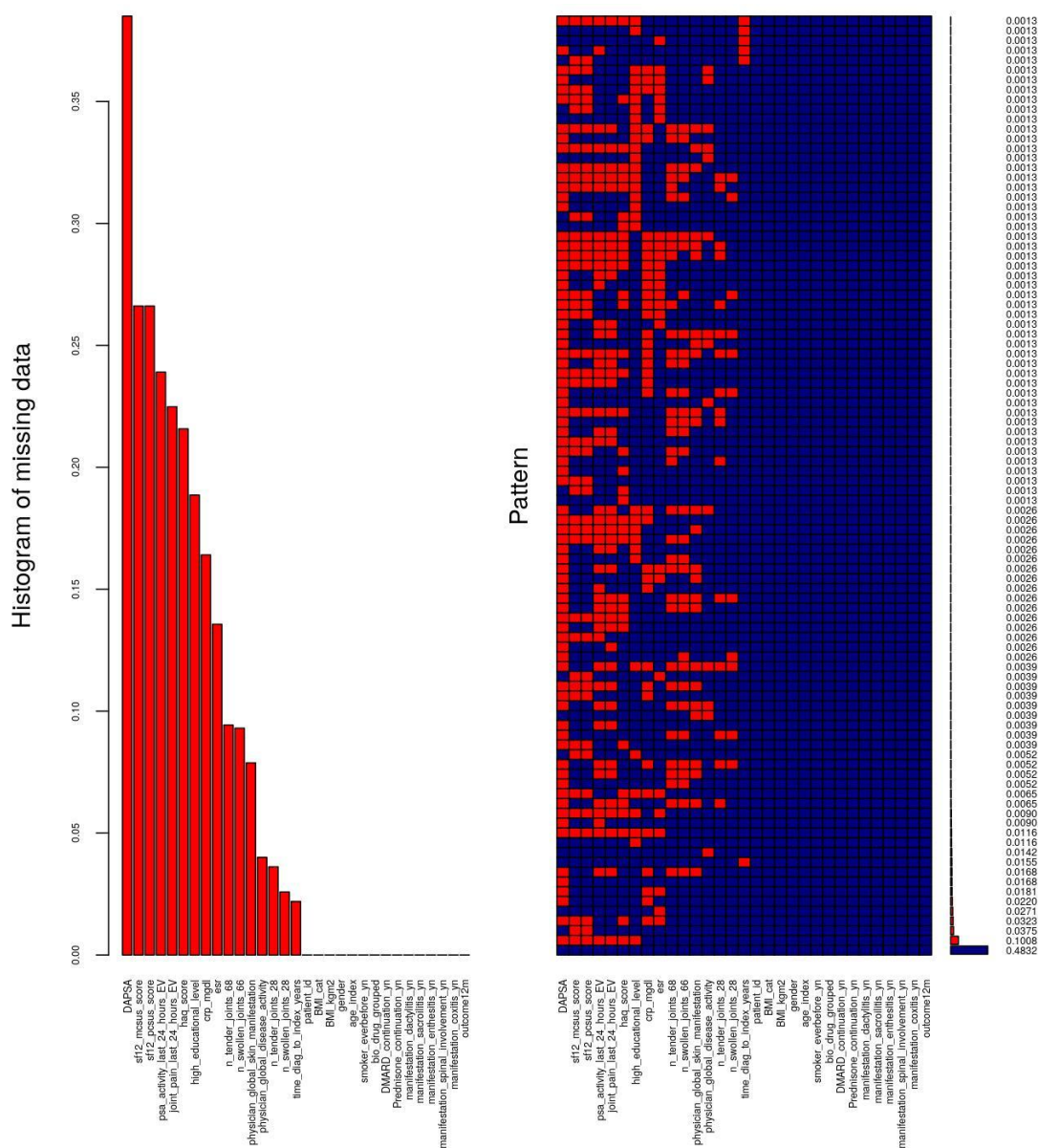
<sup>b</sup> DAPSA not used as predictor for: sjc66, tjc68, PatActv, PatPain, CRP.

<sup>c</sup> DAS28 not used as predictor for: sjc28, tjc28, ESR.

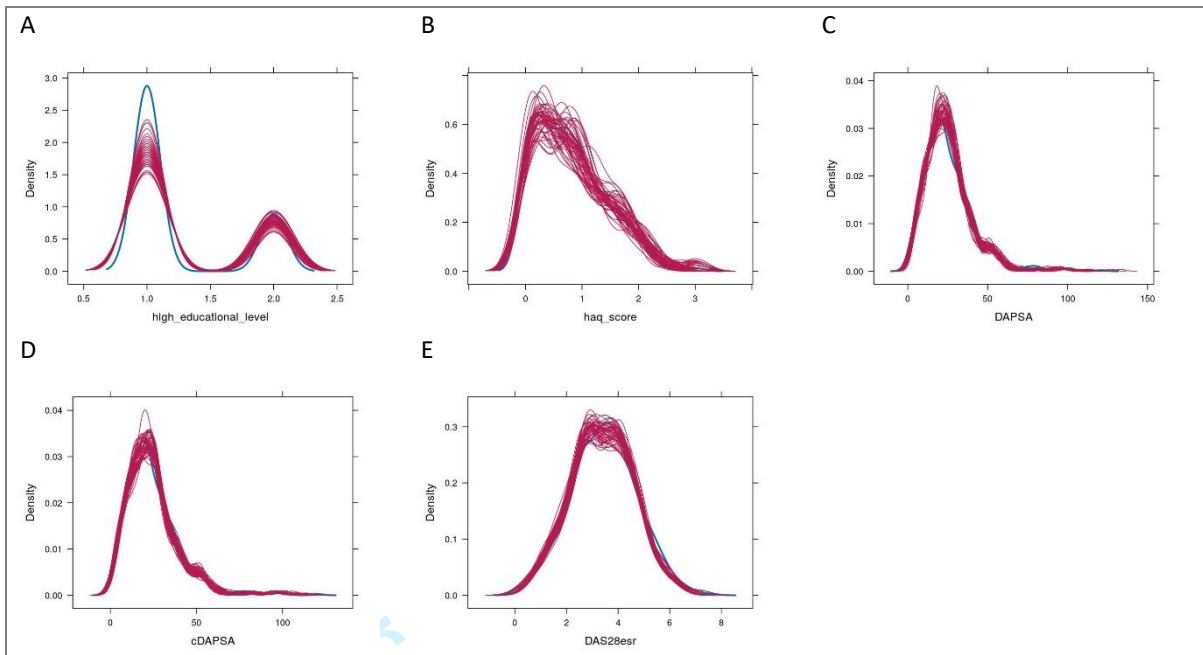
<sup>d</sup> DAPSA passive imputation:  $DAPSA = sjc66 + tjc68 + PatActv + PatPain + CRP$

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

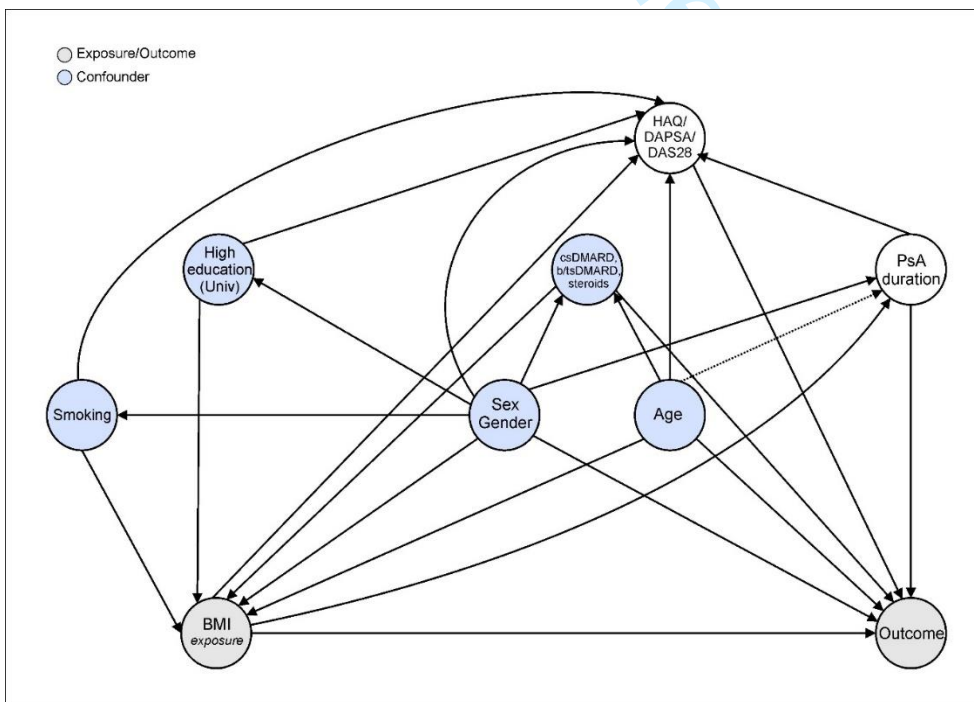




**Supplementary Figure S2.** Graphical representation of the missingness among baseline variables included in the imputations for primary analysis (i.e., achievement of Minimal Disease Activity (MDA) within the first year after index date). The 48.32% of patients had complete information on all the included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

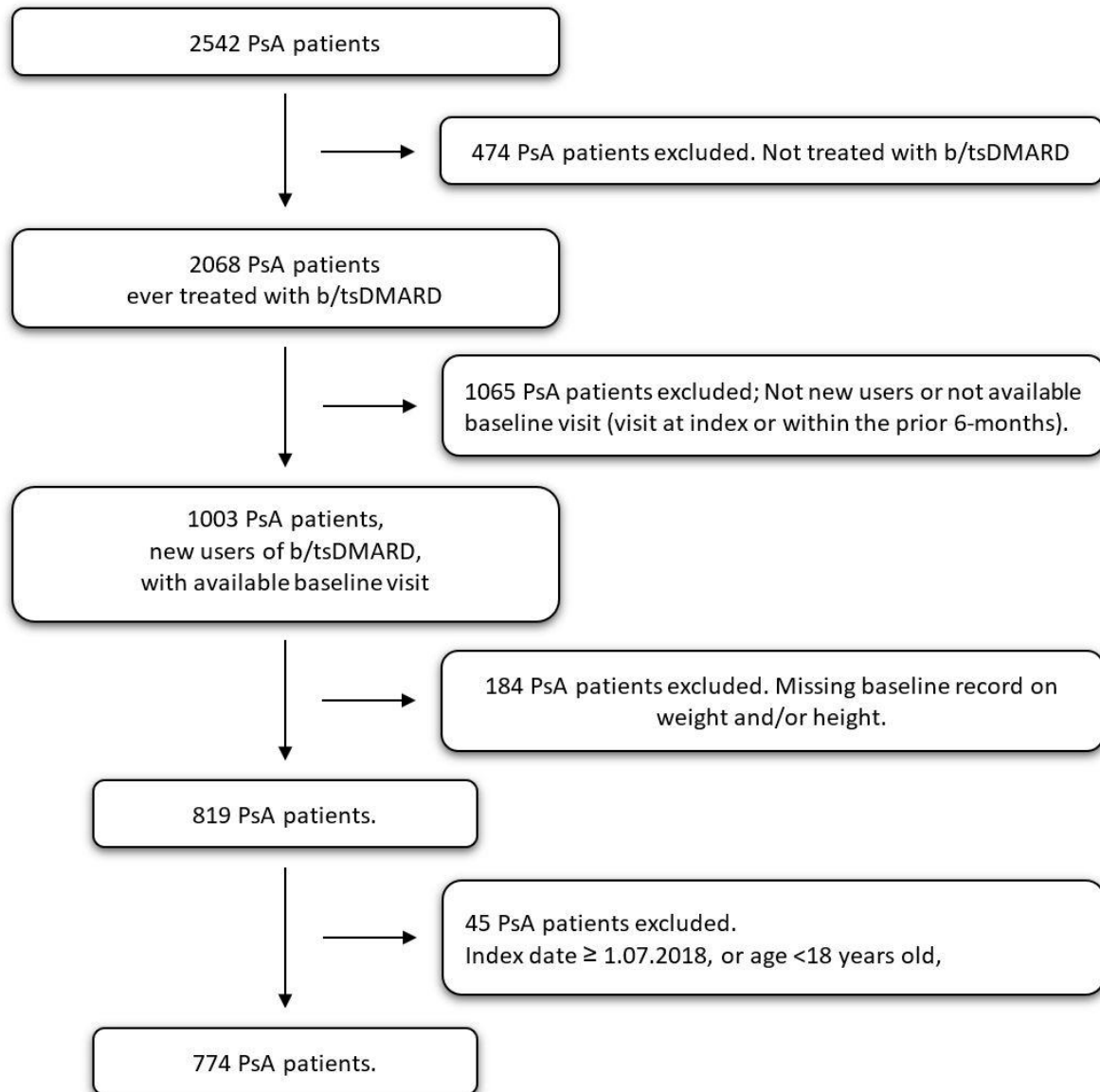


**Supplementary Figure S3.** Density plots for the imputed variables high educational level [A], Health Assessment Questionnaire (HAQ) [B], and Disease Activity Index for Psoriatic Arthritis (DAPSA) [C] for the primary outcome, achievement of Minimal Disease Activity (MDA) within the first year after 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 rationale 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 <sup>c</sup> (95% CI) | n events                    | ORadj <sup>c</sup> (95% CI) | n events                    | ORadj <sup>c</sup> (95% CI) |
| <b>MDA</b>                   |                            |                             |                             |                             |                             |                             |
| 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)             |
| <b>DAPSA-remission</b>       |                            |                             |                             |                             |                             |                             |
| 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)               |
| <b>DAPSA-remLDA</b>          |                            |                             |                             |                             |                             |                             |
| 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)            |
| <b>cDAPSA-remission</b>      |                            |                             |                             |                             |                             |                             |
| 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)             |
| <b>DAS28-remission</b>       |                            |                             |                             |                             |                             |                             |
| 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)            |
| <b>Treatment persistence</b> |                            |                             |                             |                             |                             |                             |
| 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<sup>c</sup>: odds ratio adjusting for: sex, age, high educational level, smoker, b/tsDMARD, csDMARD, corticosteroid, and HAQ (for MDA) or DAPSA (for DAPSA-remission/DAPSA-remLDA) 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 <sup>a</sup> (95% CI) | ORadj <sup>b</sup> (95% CI) | ORadj <sup>c</sup> (95% CI) |
| <b>MDA</b>              |   |          |                          |                             |                             |
| 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)            |
| <b>DAPSA-remission</b>  |   |          |                          |                             |                             |
| 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)            |
| <b>DAPSA-remLDA</b>     |   |          |                          |                             |                             |
| 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)            |
| <b>cDAPSA-remission</b> |   |          |                          |                             |                             |
| 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)            |
| <b>DAS28-remission</b>  |   |          |                          |                             |                             |
| 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<sup>c</sup>: odds ratio adjusting for: sex, age, high educational level, smoker, b/tsDMARD, csDMARD, corticosteroid, and HAQ (for MDA) or DAPSA (for DAPSA-remission/DAPSA-remLDA) 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<br>(n=774)          | Normal weight<br>(n=306) | Overweight<br>(n=285) | Obese<br>(n=183) |
| <b>MDA</b>              | 125 (16.15)                 | 66 (21.57)               | 40 (14.04)            | 19 (10.38)       |
| <b>DAPSA-remission</b>  | 83 (10.72)                  | 51 (16.67)               | 20 (7.02)             | 12 (6.56)        |
| <b>DAPSA-remLDA</b>     | 197 (25.45)                 | 84 (27.45)               | 76 (26.67)            | 37 (20.22)       |
| <b>cDAPSA-remission</b> | 112 (14.47)                 | 57 (18.63)               | 39 (13.68)            | 16 (8.74)        |
| <b>DAS28-remission</b>  | 275 (35.53)                 | 115 (37.58)              | 109 (38.25)           | 51 (27.87)       |
| <b>Persistence</b>      | 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 |          |             |           |          | Overall<br>(n=774)<br>(counts) | Normal weight<br>(n=306)<br>(counts) | Overweight<br>(n=285)<br>(counts) | Obese<br>(n=183)<br>(counts) |
|-------------------|----------|-------------|-----------|----------|--------------------------------|--------------------------------------|-----------------------------------|------------------------------|
| MDA               | DAPSArem | DAPSAremLDA | cDAPSArem | DAS28rem |                                |                                      |                                   |                              |
| ✓                 | -        | -           | -         | -        | 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**Enriqueta Vallejo-Yagüe<sup>1</sup>, Theresa Burkard<sup>1</sup>, Andrea M. Burden<sup>1</sup><sup>1</sup> Department of Chemistry and Applied Biosciences, Institute of Pharmaceutical Sciences, ETH Zurich, Zurich, Switzerland.STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

|                              | Item No | Recommendation   | Page No                       |
|------------------------------|---------|--|-------------------------------|
| <b>Title and abstract</b>    | 1       | (a) Indicate the study's design with a commonly used term in the title or the abstract<br><br>(b) Provide in the abstract an informative and balanced summary of what was done and what was found  | 1-2 (Title and abstract)<br>2 |
| <b>Introduction</b>          |         |  |                               |
| 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                             |
| <b>Methods</b>               |         |  |                               |
| 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<br><br>(b) For matched studies, give matching criteria and number of exposed and unexposed  | 5<br>NA                       |
| Variables                    | 7       | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable   | 5-7                           |
| Data sources/<br>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;<br>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<br><br>(b) Describe any methods used to examine subgroups and interactions<br><br>(c) Explain how missing data were addressed<br><br>(d) If applicable, explain how loss to follow-up was addressed<br><br>(e) Describe any sensitivity analyses | 8-9<br>8-9<br>8-9<br>7<br>7-9 |
| <b>Results</b>               |         |  |                               |

|    |                          |     |   |  |
|----|--------------------------|-----|---|--|
| 1  | 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<br>(b) Give reasons for non-participation at each stage<br>(c) Consider use of a flow diagram   | Figure 1<br>Figure 1<br>Figure 1                     |
| 2  |                          |     |   |  |
| 3  |                          |     |   |  |
| 4  |                          |     |   |  |
| 5  |                          |     |   |  |
| 6  |                          |     |   |  |
| 7  | Descriptive data         | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate number of participants with missing data for each variable of interest<br>(c) Summarise follow-up time (eg, average and total amount)  | 9<br>Table 1<br>NA (see page 7)                      |
| 8  |                          |     |   |  |
| 9  |                          |     |   |  |
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| 11 |                          |     |   |  |
| 12 |                          |     |   |  |
| 13 |                          |     |   |  |
| 14 | Outcome data             | 15* | Report numbers of outcome events or summary measures over time  | Table 2  |
| 15 |                          |     |   |  |
| 16 | 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<br>(b) Report category boundaries when continuous variables were categorized<br>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 9-11;<br>Table 2<br>6<br>(exposure and outcome)<br>- |
| 17 |                          |     |   |  |
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| 26 | Other analyses           | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses  | 10   |
| 27 |                          |     |   |  |
| 28 |                          |     |   |  |
| 29 | <b>Discussion</b>        |     |   |  |
| 30 | Key results              | 18  | Summarise key results with reference to study objectives  | 11   |
| 31 |                          |     |   |  |
| 32 | 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  |
| 33 |                          |     |   |  |
| 34 | 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  |
| 35 |                          |     |   |  |
| 36 | Generalisability         | 21  | Discuss the generalisability (external validity) of the study results   | -  |
| 37 |                          |     |   |  |
| 38 | <b>Other information</b> |     |   |  |
| 39 | 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   | -  |
| 40 |                          |     |   |  |
| 41 |                          |     |   |  |

\*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>.

# BMJ Open

## 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

|                                 |  |
|---------------------------------|--|
| Journal:                        | <i>BMJ Open</i>  |
| Manuscript ID                   | bmjopen-2022-061474.R1   |
| Article Type:                   | Original research  |
| Date Submitted by the Author:   | 13-Jun-2022  |
| Complete List of Authors:       | Vallejo-Yagüe, Enriqueta; ETH Zürich, Institute of Pharmaceutical Sciences, Department of Chemistry and Applied Biosciences<br>Burkard, Theresa; ETH Zürich, Institute of Pharmaceutical Sciences, Department of Chemistry and Applied Biosciences<br>Micheroli, Raphael; University Hospital of Zurich, University of Zurich, Department of Rheumatology<br>Burden, Andrea; ETH Zurich, Institute of Pharmaceutical Sciences, Department of Chemistry and Applied Biosciences |
| <b>Primary Subject Heading</b>: | Rheumatology   |
| Secondary Subject Heading:      | Epidemiology   |
| Keywords:                       | RHEUMATOLOGY, EPIDEMIOLOGY, Rheumatology < INTERNAL MEDICINE   |
|                                 |  |

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3 1 **Minimal Disease Activity and remission in psoriatic arthritis**  
4 **patients with elevated body mass index: an observational cohort**  
5 **study in the Swiss Clinical Quality Management cohort**  
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8

9 4 Enriqueta Vallejo-Yagüe<sup>1</sup>, Theresa Burkard<sup>1</sup>, Raphael Micheroli<sup>2</sup>, Andrea M. Burden<sup>1</sup>  
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34 24 **Keywords:** psoriatic arthritis; minimal disease activity; remission; obesity; body mass index.  
35  
36  
37 25  
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39 26 Abstract word count: 293

40 27 Manuscript word count: 3430  
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## 30 ABSTRACT

31 **Objective:** To assess the impact of elevated body mass index (BMI) in the achievement of  
32 Minimal Disease Activity (MDA) and several definitions of remission in PsA patients in  
33 Switzerland. Secondly, to assess the overlapping across the study outcomes.

34 **Methods:** This observational cohort study in the Swiss Clinical Quality Management in  
35 Rheumatic Diseases (SCQM) registry included PsA patients starting their first biologic or  
36 targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) from 1997 to  
37 30.06.2018. Exposure was BMI category at b/tsDMARD start: overweight, obese, and normal  
38 weight (reference). Logistic regression was used to assess the achievement of MDA and  
39 remission at  $\leq 12$ -months, as well as treatment persistence at one-year, in overweight and obese  
40 patients compared to the normal weight group. Remission was defined by Disease Activity for  
41 Psoriatic Arthritis (DAPSA), clinical DAPSA (cDAPSA), and 28-joint disease activity score  
42 (DAS28). Additionally, overlapping across study outcomes was investigated.

43 **Results:** The study included 306 (39.5%) normal weight, 285 (36.8%) overweight, and 183  
44 (23.6%) obese patients. Compared to the normal weight group, obese patients had lower odds  
45 of achieving MDA at  $\leq 12$ -months (Adjusted odds ratio [OR<sub>adj</sub>] 0.45, 95% confidence interval  
46 [CI] 0.24-0.82). This was consistent with the observed reduced odds of achieving DAPSA-  
47 remission (OR<sub>adj</sub> 0.42, 95%CI 0.21-0.85), cDAPSA-remission (OR<sub>adj</sub> 0.51, 95%CI 0.27-  
48 0.96), and DAS28-remission (OR<sub>adj</sub> 0.51, 95%CI 0.32-0.81) in obese vs normal weight  
49 patients. Among the 125 patients achieving MDA, the majority (81.8% normal weight, 80.0%  
50 overweight, 78.9% obese) achieved cDAPSA-remission. No differences were observed in the  
51 odds to achieving treatment persistence between the BMI strata.

52 **Conclusions:** Obesity halved the likelihood of achieving MDA and remission in PsA patients  
53 with b/tsDMARDs compared to those with normal weight, while it did not impact treatment  
54 persistence. High overlapping of patients achieving the outcomes MDA and cDAPSA-  
55 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.

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58

## 59 INTRODUCTION

60 Psoriatic arthritis (PsA) is an immune-mediated rheumatic disease,<sup>1</sup> with an estimated  
61 prevalence of 0.05-0.42%,<sup>2-4</sup> and 5-41% among patients with psoriasis.<sup>3</sup> PsA is a complex and  
62 multifactorial disease,<sup>5</sup> for which pathological features include musculoskeletal involvement,  
63 such as inflammation of the peripheral joints (arthritis), the entheses (enthesitis), the axial  
64 skeleton (spondylitis), and the finger and toe digits (dactylitis), as well as extra-articular  
65 manifestations involving skin and nails, and potentially other organs.<sup>6</sup> Pharmacological  
66 treatments include conventional synthetic disease-modifying anti-rheumatic drugs  
67 (csDMARDs) and biologic or targeted synthetic disease-modifying anti-rheumatic drugs  
68 (b/tsDMARDs).<sup>3</sup> Treatment of PsA aims to maximise health-related quality of life (QoL),  
69 through targeting symptoms and structural damage,<sup>7</sup> and it is recommended to target  
70 low/minimal disease activity or remission.<sup>6</sup>

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

78 The rationale behind the association between obesity and PsA has been previously  
79 discussed.<sup>5,17,18</sup> In short, obesity has been described as a low-grade inflammatory disease,<sup>18</sup> and  
80 both obesity and PsA share pathological inflammatory pathways.<sup>5,18,19</sup> Further evidence  
81 supporting the association between obesity and a worse PsA clinical outcome is the association  
82 of weight loss with higher rate of achieving MDA.<sup>20</sup> Additionally, obesity is a well-known  
83 contributor to the metabolic syndrome (MetS), and MetS was similarly associated to lower  
84 likelihood of achieving MDA in PsA patients.<sup>21</sup>

1  
2 85 Despite the growing evidence on the association between obesity and worse clinical  
3  
4 86 response in PsA patients, most published observational cohort studies on this topic had  
5  
6 87 relatively small sample size. For example, a systematic review investigating the association  
7  
8 88 between obesity and response in immune-mediated inflammatory diseases identified one  
9  
10 89 randomised clinical trial and eight observational cohort studies in PsA patients, but six of the  
11  
12 90 included observational cohorts had a sample size  $\leq 330$ .<sup>16</sup> Thus, further investigating this effect,  
13  
14 91 especially in a different and bigger population cohort, remains of interest. Additionally, it is  
15  
16 92 unclear whether the findings would remain consistent across outcome definitions.  
17  
18  
19

20 93 Thus, we seek to contribute to the growing body of evidence by performing an  
21  
22 94 observational cohort study aiming to assess the impact of BMI in the achievement of MDA and  
23  
24 95 remission in PsA patients. Additionally, by including several outcome definitions we aim to  
25  
26 96 investigate the consistency of the findings when considering different aspects of the disease.  
27  
28  
29

## 30 97 **METHODS**

### 31 98 **Study design and data source**

32  
33 99 We performed an observational cohort study in the Swiss Clinical Quality Management in  
34  
35 100 Rheumatic Diseases (SCQM) registry from January 1<sup>st</sup> 1997 and July 31<sup>st</sup> 2019. The SCQM is  
36  
37 101 a national longitudinal population-based cohort of rheumatic diseases in Switzerland, initiated  
38  
39 102 in 1997.<sup>22</sup> SCQM data are recorded during routine clinical practice, and includes information  
40  
41 103 on demographics, body height and weight, life-style habits, anti-rheumatic medication (with  
42  
43 104 start and stop dates), clinical endpoints, patient-reported outcomes, and health standardized  
44  
45 105 surveys.<sup>12,22</sup> Diagnosis of PsA is recorded in SCQM following the physician's criteria.  
46  
47  
48  
49

### 50 106 **Study population**

51  
52 107 PsA patients ( $\geq 18$  years old) starting their first b/tsDMARD in the SCQM registry between  
53  
54 108 June 1<sup>st</sup> 2020 and June 30<sup>th</sup> 2018 (inclusive) were included in the study. The first recorded start  
55  
56 109 of b/tsDMARD in the SCQM was defined as the index date. Patients with a b/tsDMARD start  
57  
58  
59  
60

1  
2 110 date before their first registered visit at SCQM were excluded. Similarly, patients without a  
3  
4 111 baseline record on height and weight were excluded.

## 6 112 **Exposure**

8  
9 113 The exposure of interest was BMI category at the start of the patients' first b/tsDMARD.  
10  
11 114 Baseline BMI ( $\text{kg}/\text{m}^2$ ) was calculated using height and weight records (**Supplementary**  
12  
13 115 **Equation 1**) at index date or as close as possible to this date within a 6-month look-back  
14  
15 116 window. Patients were classified based on BMI as normal weight ( $\text{BMI} < 25$ ), overweight ( $\text{BMI}$   
16 117  $25.0-29.9$ ), and obese ( $\text{BMI} \geq 30$ ). The normal weight group was the reference category.

## 20 118 **Outcomes**

22  
23 119 The primary outcome was defined as achievement of MDA within the first year after the index  
24  
25 120 date. MDA was achieved if at least five of the following seven criteria were met: number of  
26  
27 121 tender joint counts (TJC)  $\leq 1$ ; number of swollen joint counts (SJC)  $\leq 1$ ; skin manifestation none  
28  
29 122 or almost none; patient's joint pain by visual analogue scale (VAS, 0-100)  $\leq 15$ ; patient's  
30  
31 123 assessment on PsA activity by VAS  $\leq 20$ ; Health Assessment Questionnaire (HAQ)  $\leq 0.5$ ;  
32  
33 124 enthesitis points  $\leq 1$ .<sup>23</sup>

36 125 Secondary outcomes assessed within the first year were: achievement of Disease  
37  
38 126 Activity for Psoriatic Arthritis (DAPSA) remission, defined as  $\text{DAPSA} \leq 4$ ; DAPSA remission  
39  
40 127 or low disease activity (DAPSA-remLDA), defined as  $\text{DAPSA} \leq 14$ ; clinical DAPSA  
41  
42 128 (cDAPSA) remission, defined as  $\text{cDAPSA} \leq 4$ ; and 28-joint disease activity score (DAS28)  
43  
44 129 remission, defined as  $\text{DAS28} < 2.6$ . DAPSA, cDAPSA, and DAS28 formulas are described in  
45  
46 130 the **Supplementary Equations 2-5**. DAS28-remission was calculated using erythrocyte  
47  
48 131 sedimentation rate (ESR; DAS28-ESR), however, in cases where follow-up data on DAS28-  
49  
50 132 ESR was missing, DAS28 with C-reactive protein (CRP; DAS28-CRP) was used instead, if  
51  
52  
53  
54  
55 133 available.

1  
2 134 As a tertiary outcome, persistence with the first b/tsDMARD at the end of month-12 was  
3  
4 135 assessed. We allowed for a permissible gap of one-month between treatment courses of the  
5  
6 136 same b/tsDMARD, as illustrated in the **Supplementary Figure S1**.

8  
9 137 Patients with missing information on the study outcomes during the follow-up were  
10  
11 138 categorized as not having achieved the corresponding outcome. In a sensitivity analysis, we re-  
12  
13 139 ran our analyses excluding patients with missing information on outcome during follow-up.

#### 140 **Follow-up**

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

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

#### 148 **Covariates**

149 Baseline variables included demographics, BMI, high education, ever smoking, anti-rheumatic  
150 medication (i.e., b/tsDMARD, csDMARD, corticosteroid), inflammatory markers or acute  
151 phase reactants (i.e., ESR, CRP), physician's assessment on disease activity and skin, patient-  
152 reported disease activity and pain, tender and swollen joint counts (counting 28 joints),  
153 composite disease activity scores (i.e., DAPSA, cDAPSA, DAS28-ESR), disease-specific  
154 manifestations (i.e., musculoskeletal manifestations, dactylitis, enthesitis, sacroilitis, spinal  
155 involvement, coxitis, peripheral arthritis, nail manifestation), health standardized surveys (i.e.,  
156 Health Assessment Questionnaire [HAQ], Short Form-12 [SF-12]), and comorbidities (i.e.,  
157 cardiovascular event/disease, diabetes or other metabolic problems, depression/anxiety).  
158 Baseline variables were collected at index date, or as close as possible to that date within a 6-  
159 month look-back window, except for: composite disease activity scores, disease-specific

1  
2 160 manifestations, and health standardised surveys, which were collected with a 3-months look-  
3  
4 161 back window. Information on smoking, cardiovascular event/disease, and diabetes, which was  
5  
6 162 included if ever reported prior or at index date. Anti-rheumatic medication which was collected  
7  
8  
9 163 on the index date.

## 10 164 **Data analysis**

11  
12  
13 165 Patient baseline characteristics were described, and the overweight and obese categories were  
14  
15 166 compared to the normal weight group (reference group) using chi-squared test for categorical  
16  
17 167 variables and t-test, ANOVA, or Kruskal-Wallis test for continuous variables. For these tests,  
18  
19 168 missing values did not function as a grouping variable. Statistical significance was defined as  
20  
21 169  $p \leq 0.05$ .

22  
23  
24  
25 170 Subsequently, missingness for key baseline variables was addressed with multiple  
26  
27 171 imputation by chained equation (MICE) using the *mice* package<sup>24</sup> in the R Statistical  
28  
29 172 Software.<sup>25</sup> MICE was performed for each study outcome separately, using 50 imputations with  
30  
31 173 15 interactions for each set. Variables included in the imputations, their original missingness,  
32  
33 174 and corresponding applied imputation models are presented in the **Supplementary Table S1**.  
34  
35 175 The 48.32% of the study population had complete information on every variable included in  
36  
37 176 the MICE for the main analysis (**Supplementary Figure S2**). Convergence of imputations was  
38  
39 177 assessed by visual inspection of density plots (**Supplementary Figure S3**).

40  
41  
42  
43 178 To investigate the association between BMI categories and the study outcomes,  
44  
45 179 multivariable logistic regression models were conducted (outcome specific) for individual  
46  
47 180 imputed datasets, and the results were pooled to a single estimate according to Rubin's rules.  
48  
49 181 These models were conducted first, including only sex and age as covariates, and second,  
50  
51 182 adding clinical confounders (full-adjusted). Confounders were chosen based on clinical  
52  
53 183 rational and direct acyclic graphs (DAGs) (**Supplementary Figure S4**), and included: sex  
54  
55 184 (male; female), age, high education (yes/no), ever smoking (yes/no), b/tsDMARD (TNFi; other  
56  
57 185 biologic; tsDMARD), csDMARD at index date (yes/no), and corticosteroid use at index date  
58  
59  
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1  
2 186 (yes/no). Additionally, sensitivity analyses were performed whereby we added the respective  
3  
4 187 composite disease activity score or health standardized survey to the fully adjusted models for  
5  
6 188 primary and secondary outcomes to assess their potential mediating impact on the analyses.  
7  
8  
9 189 Another sensitivity analysis addressed the one-year outcomes after excluding patients with  
10  
11 190 underweight (BMI<18.5 kg/m<sup>2</sup>)

12  
13 191 Lastly, to compare the overlapping across study outcomes, the proportion of patients  
14  
15 192 achieving each outcome (per BMI group) was summarised, and the overlapping of patients  
16  
17 193 achieving individual primary and secondary outcomes during the first year was illustrated with  
18  
19 194 a Venn Diagram.

### 20 195 **Patient and Public Involvement**

21  
22 196 Patients or the public were not involved in the design, or conduct, or reporting, or dissemination  
23  
24  
25 197 plans of our research.

## 26 198 **RESULTS**

27  
28 199 The study included 774 adult PsA patients starting their first b/tsDMARD. **Supplementary**  
29  
30 200 **Figure S5** illustrates the cohort selection process. Among included patients, 306 (39.53%) were  
31  
32 201 normal weight, 285 (36.82%) were overweight, and 183 (23.64%) were obese. Baseline patient  
33  
34 202 characteristics (prior to imputation) are presented in **Table 1**. Compared to the normal weight  
35  
36 203 group, overweight patients had higher SJC, were less frequently women, and had older mean  
37  
38 204 age. Both overweight and obese patients had lower frequency of high education, and higher  
39  
40 205 patient-reported disease activity and joint pain, while only obese patients had higher CRP  
41  
42 206 levels. Compared to the normal weight category, DAPSA and DAS28 were elevated in the  
43  
44 207 overweight group, while cDAPSA was higher in both overweight and obese BMI categories.  
45  
46 208 HAQ and SF-12 with physical components (SF-12pcs) were worse in the obese patients, and  
47  
48 209 patients with obesity were more likely to have had a cardiovascular event/disease than the  
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50 210 normal weight group.

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**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<br>(n=306) | Overweight<br>(n=285) | p-value | Obese<br>(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<sup>2</sup>); Overweight (BMI 25.0-29.9 kg/m<sup>2</sup>); Obese (BMI ≥30 kg/m<sup>2</sup>). 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.

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215 Results from the logistic regression for the primary analysis are presented in **Figure 1**.

216 Compared to the normal weight group, obese patients had significantly lower odds of achieving

217 MDA within the first year, with an adjusted Odds Ratio (OR<sub>adj</sub>) of 0.45 (95% confidence

218 interval [CI] 0.24-0.82). Similarly, both overweight and obese patients had >50% reduced odds

219 of achieving DAPSA-remission (overweight OR<sub>adj</sub> 0.44 [95% CI 0.24-0.79] and obese OR<sub>adj</sub>

220 0.42 [95% CI 0.21-0.85]), compared to normal weight patients. Additionally, obese patients

221 had reduced odds of achieving cDAPSA-remission (OR<sub>adj</sub> 0.51 [95% CI 0.27-0.96]) and

222 DAS28-remission (OR<sub>adj</sub> 0.51 [95% CI 0.32-0.81]) within the first year. No differences were

223 observed across BMI categories on achievement of DAPSA-remLDA or treatment persistence

224 at the end of month-12.

225 The secondary analyses showed that extending the maximum follow-up to 15-months

226 resulted in similar findings to those from the 12-months analyses (**Table 2**). However, in the

227 9-months analyses, the associations of obesity with DAPSA-remission and with cDAPSA-

228 remission were no longer significant (**Table 2**).

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

|  | n<br>sample<br>size | Maximum follow-up 9-months |                  |                  | Maximum follow-up 15-months |                  |                  |
|--|---------------------|----------------------------|------------------|------------------|-----------------------------|------------------|------------------|
|  |                     | n<br>vents                 | OR               | ORadj            | n<br>events                 | OR               | ORadj            |
| <b>MDA</b>   |                     |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>DAPSA-remission</b>                               |                     |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>DAPSA-remLDA</b>                                  |                     |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>cDAPSA-remission</b>                              |                     |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>DAS28-remission</b>                               |                     |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>Treatment persistence at the end of follow-up</b> |                     |                            |                  |                  |                             |                  |                  |
| 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.

236  
 237 In the sensitivity analysis in which the respective composite disease activity score or  
 238 health standardized survey was included in the model, the previously observed findings in the  
 239 high BMI groups were attenuated, with the exception of obesity and achievement of MDA  
 240 (**Supplementary Table S2**). The sensitivity analysis excluding patients with missing  
 241 information on outcome during the one-year follow-up yielded stronger reduced odds of  
 242 achieving MDA and remission among abnormal BMI categories vs the normal weight group  
 243 (**Supplementary Table S3**). The sensitivity analysis excluding the 12 patients with BMI<18.5  
 244 yielded similar results to the main study findings (**Supplementary Table S4**).

1  
2 245 The frequency of achieved outcomes (with 12-months follow-up) per BMI category are  
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4 246 presented in **Figure 2**. Overall, 125 patients achieved MDA, 83 DAPSA-remission, 197  
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6 247 DAPSA-remLDA, 112 cDAPSA-remission, and 275 DAS28-remission within the first year.  
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8 248 Across all outcomes, patients with obesity had a lower prevalence of achieved outcomes.  
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10 249 DAS28-remission and treatment persistence had the highest prevalence in all groups, with  
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12 250 37.58% and 59.80% achieved among normal weight patients and 27.87% and 51.37% among  
13  
14 251 obese, respectively.  
15  
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17  
18 252 The overlap of patients achieving the outcomes during the first year is illustrated in  
19  
20 253 **Figure 3**, complemented with numerical values in **Supplementary Table S5**. Among the 125  
21  
22 254 patients achieving MDA (66 normal weight, 40 overweight, 19 obese), 80 also achieved  
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24 255 DAPSA-remission, of which 48 (72.73%) were normal weight, 20 (50.00%) were overweight,  
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26 256 and 12 (63.16%) were obese. Similarly, among patient with MDA, 54 (81.82%) normal weight,  
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28 257 32 (80.00%) overweight, and 15 (78.95%) obese patients also achieved cDAPSA-remission.  
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30 258 Additionally, MDA overlapped with every remission outcome in 45 (68.18%) normal weight,  
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32 259 18 (45.00%) overweight, and 11 (57.89%) obese patients.  
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## 37 260 **DISCUSSION**

38  
39 261 This observational cohort study found that obese patients had a significant 49% to 58% reduced  
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41 262 odds of achieving MDA, DAPSA-remission, cDAPSA-remission, and DAS28-remission  
42  
43 263 within the first year, when compared to normal weight patients. Conversely, being overweight  
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45 264 was only associated with a reduced odds of achieving DAPSA remission. In both high BMI  
46  
47 265 categories, the association with achievement of DAPSA-remLDA within the first year and with  
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49 266 one-year treatment persistence, were not statistically significant. Among patients who achieved  
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51 267 MDA, the majority also achieved cDAPSA-remission.  
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54  
55 268 Our findings on the association between obesity and lower probability of reaching MDA  
56  
57 269 and remission are consistent with other longitudinal observational studies.<sup>10,13,15</sup> In the  
58  
59 270 prospective study by Di Minno et al., obesity was associated with increased risk of not  
60

1  
2 271 achieving MDA during a 12-months follow-up compared to patients with BMI<30 (hazard  
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4 272 ratio 4.90, 95%CI 3.04–7.87).<sup>13</sup> Eder et al. reported that, compared to normal weight patients  
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6 273 (BMI<25), overweight and obese patients had 34% and 47% significantly reduced odds of  
7  
8 274 achieving MDA, respectively.<sup>10</sup> While we identified a similar OR in the overweight and obese  
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10 275 patients, our results in the overweight group were not statistically significant. In the study by  
11  
12 276 Højgaard et al., obesity was associated with 53% lower odds of achieving European Alliance  
13  
14 277 of Associations for Rheumatology (EULAR) good or moderate (EGOM) response.<sup>15</sup> While we  
15  
16 277 did not assess EGOM response, this is a DAS28-driven outcome, and the findings are in  
17  
18 278 agreement with our observed association between obesity and 49% reduced odds for DAS28-  
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20 279 remission. Conversely, Iannone et al. suggested no significant differences in DAS28-remission  
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22 280 rates across BMI categories.<sup>26</sup> However, they had a small sample size (135 patients), and their  
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24 281 observed lower remission rate in the obese vs normal weight patients was in line with our  
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26 282 findings.  
27  
28 283

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30 284 Additionally, results from Højgaard et al. showed that compared to non-obese patients  
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32 285 (BMI<30), obese patients were associated with a 60% higher risk of TNFi discontinuation  
33  
34 286 during their study period (median follow-up of 1.5 years).<sup>15</sup> While our study did not yield an  
35  
36 287 association between BMI and treatment persistence, these contrasting findings may be  
37  
38 288 explained by the different methodologies. Højgaard et al. assessed the time to withdrawal using  
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40 289 a survival model, which gives high attention to early outcomes, while we investigated  
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42 290 persistence yes/no at a specific timepoint using logistic regression.  
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47

48 291 In our study, MDA was the main outcome as it covers several aspects from the disease  
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50 292 presentation and consequences, and has been associated with patient's QoL and productivity.<sup>27</sup>  
51  
52 293 Additionally, McGagh and Coates suggested that the 66/68 joint counts provides a more  
53  
54 294 realistic picture of joint involvement in PsA, compared to the 28 joint counts, and highlighted  
55  
56 295 the benefits of including patient-reported outcomes.<sup>28</sup> Based on this, we identified DAPSA-  
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58 296 remission and cDAPSA-remission as optimal secondary outcomes. However, we expect that  
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60

1  
2 297 cDAPSA may be a better fit to study patients with abnormal BMI since obesity was associate  
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4 298 with elevated CRP in the general population.<sup>29–31</sup> This is further supported by the high overlap  
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6 299 of patients achieving MDA and cDAPSA-remission in our study, which was similar across  
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8  
9 300 every BMI group.

10  
11 301 Regarding the observed higher frequency of achievement of DAS28-remission compared  
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13 302 to other remission endpoints, this may be explained by its narrow focus on peripheral  
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15 303 manifestations, potentially underestimating residual disease activity. Nevertheless, the  
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17 304 consistency of the observed results on MDA and remission outcomes in the obese group  
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19 305 suggests that obesity affects peripheral joints, as well as disease-specific manifestations and  
20  
21 306 the patient's perspective. However, we note that the different outcome definitions led to  
22  
23 307 contrasting results in the overweight group, suggesting that the effect of overweight on the PsA  
24  
25 308 may not be fully captured by every remission definition. Similarly, the impact of obesity on  
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27 309 PsA clinical response was not consistent with the more clinically accessible outcome low  
28  
29 310 disease activity (DAPSA-remLDA).

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33  
34 311 The reasons for the lower response rates in obese patients could be multiple. High body  
35  
36 312 weight can affect the clearance and volume of distribution of b/tsDMARDs.<sup>32–34</sup> Adipose tissue  
37  
38 313 has a proinflammatory capacity,<sup>35</sup> which could negatively influence drug response. Finally, a  
39  
40 314 relationship between mechanical stress and triggering of musculoskeletal inflammation (deep  
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42 315 Köbner phenomenon) in psoriatic arthritis is discussed. Nevertheless, the observed lower odds  
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44 316 of achieving MDA or remission in the obese group is of interest, and the consistency across  
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46 317 the studied definitions of remission suggests that this effect may be reflected on several factors  
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48 318 of the PsA disease.

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52 319 Finally, as described elsewhere,<sup>12</sup> the prevalence of overweight and obesity were higher  
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54 320 among PsA patients in comparison to the general population in Switzerland (Switzerland 2017,  
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56 321 people >15 years old, 31% overweight and 11% obese).<sup>36</sup> Higher obesity prevalence among  
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58 322 PsA patients in comparison to the reference population was in agreement with prior studies.<sup>12</sup>  
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60



## 323 **Strengths and limitations**

324 In addition to the large sample size and availability of BMI information (often lacking in real-  
325 world-data), the key strength of this study is the use of several relevant clinical outcome  
326 definitions. While multiple approaches to assess PsA disease activity exist, no single one has  
327 been identified as sufficient<sup>37</sup> and the choice of the optimal measure remains challenging.<sup>28</sup> The  
328 consistency of the observed results on MDA and remission outcomes in the obese group  
329 reinforces the study findings. However, we did not look at unidimensional outcomes (e.g.,  
330 dactylitis) and this remains of interest for future studies. Additionally, while standard MDA  
331 definition includes Psoriasis Activity and Severity Index (PASI)  $\leq 1$  or body surface area (BSA)  
332  $\leq 3$ ,<sup>38</sup> due to data restrictions our MDA definition included a skin manifestation of “none” or  
333 “almost none”, as reported by the physician.

334 Intrinsic to real-world-data, missingness was a limitation. We addressed missingness at  
335 baseline with multiple imputation and missingness during follow-up with sensitivity analyses.  
336 Our results were mainly consistent among various sensitivity analyses. For example, in the  
337 secondary analysis excluding patients who missed information on the outcome during follow-  
338 up (instead of treating them as non-achievers of the respective outcome), supported the  
339 observed effect of obesity towards MDA and remission, which was even accentuated in this  
340 sensitivity analysis. Among secondary analyses varying the duration of follow-up, the 15-  
341 month analyses showed consistence with the main findings, and the reduced effect found in the  
342 9-months analyses may be explained by higher missingness of outcome information at shorter  
343 follow-up, and therefore lower number of observed events overall.

344 Limitations to consider when interpreting the results include the potential  
345 misclassification of patients in the BMI categories. While overweight and obesity are  
346 commonly defined by BMI,<sup>39,40</sup> this lacks information on body composition. Thus, although  
347 data on waist circumference, skinfold thickness, and bioelectrical impedance may provide a  
348 better patient classification, this information is extremely limited in real-world data.

1  
2 349 Additionally, we classified patients with BMI<25 as normal weight, including patients with  
3  
4 350 BMI<18.5, who may be classified as underweight. This was done due to low prevalence of  
5  
6 351 underweight PsA patients in SCQM<sup>12</sup> and is consistent with previous practice in PsA<sup>10,26</sup> and  
7  
8  
9 352 other inflammatory rheumatic diseases research in which the majority of studies combine  
10  
11 353 normal and underweight patients.<sup>41</sup>  
12

13 354 It was suggested that obese patients may benefit from other non-TNFi b/tsDMARDs,  
14  
15 355 however, the evidence is limited.<sup>42</sup> Nevertheless, our results of a lower odds of achieving  
16  
17 356 remission may be largely driven by the high TNFi use in our cohort.  
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19

20 357 Finally, since weight loss in overweight and obese patients was identified as a predictor  
21  
22 358 of MDA achievement,<sup>20</sup> it remains of interest to perform a similar study to this one but  
23  
24 359 stratifying the overweight and obese patients by those with and without weight loss.  
25  
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## 28 360 **CONCLUSION**

29  
30 361 This study suggests that obesity in PsA patients is associated with at least a 50% reduction in  
31  
32 362 the likelihood of achieving MDA or remission within the first year after starting b/tsDMARD  
33  
34 363 therapy, when compared to normal weight patients. The consistency of findings across  
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36 364 definitions of remission suggests that obesity affects several factors of PsA disease.  
37  
38 365 Conversely, obesity was neither associated with the likelihood of achieving low disease activity  
39  
40 366 nor with treatment persistence. Finally, comparative analyses of b/tsDMARDs within BMI  
41  
42 367 groups is of interest and investigating the benefits of losing weight in this population remains  
43  
44 368 of interest.  
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## 50 369 **Author Contributions**

51  
52 370 E.V.-Y., T.B., and A.M.B. contributed to the study conceptualization and methodology; E.V.-  
53  
54 371 Y. performed data curation, formal analysis, visualization, and investigation; E.V.-Y. wrote the  
55  
56 372 original draft manuscript, and T.B., R.M., and A.M.B. contributed with revision and editing.  
57  
58 373 All authors read and agreed to the published version of the manuscript.  
59  
60



## 374 **Funding**

375 Not applicable. This research received no external funding.

## 376 **Conflict of interests**

377 None declared.

## 378 **Ethics approval**

379 This study was reviewed by the ethics commission of the Canton of Zurich (KEK: Req-2020-  
380 00045). Pseudonymized data, without access to the code key, was provided by the Swiss  
381 Clinical Quality Management in Rheumatic Diseases (SCQM) registry to the researchers.  
382 Therefore, the commission waived the need for a full ethics authorization.

## 383 **Patient consent for publication**

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

## 387 **Data Availability Statement**

388 Data belong to the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) and  
389 are available only with the approval and permission from the license holder (SCQM).

## 390 **Acknowledgments**

391 We thank all patients and rheumatologists contributing to the SCQM registry, as well as the  
392 entire SCQM staff. A list of rheumatology offices and hospitals which contribute to the SCQM  
393 registry can be found at <http://www.scqm.ch/institutions>. A list of financial supporters of  
394 SCQM can be found at <http://www.scqm.ch/sponsors>. We would like to add a personal thank  
395 you to Axel Finckh (University Hospitals of Geneva) for his input regarding the database. AMB  
396 acknowledges that her professorship is partly endowed by the Swiss National Pharmacy  
397 Association (PharmaSuisse) and the ETH Foundation.

## 398 **Supplementary Material**

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### 408 **REFERENCES**

- 409 1 Kumthekar A, Ogdie A. Obesity and Psoriatic Arthritis: A Narrative Review. *Rheumatol*  
410 *Ther* 2020; **7**: 447–56.
- 411 2 Salaffi F, De Angelis R, Grassi W, MArche Pain Prevalence, INvestigation Group  
412 (MAPPING) study. Prevalence of musculoskeletal conditions in an Italian population  
413 sample: results of a regional community-based study. I. The MAPPING study. *Clin Exp*  
414 *Rheumatol* 2005; **23**: 819–28.
- 415 3 Ogdie A, Weiss P. The Epidemiology Psoriatic Arthritis. *Rheum Dis Clin North Am* 2015;  
416 **41**: 545–68.
- 417 4 Scotti L, Franchi M, Marchesoni A, Corrao G. Prevalence and incidence of psoriatic  
418 arthritis: A systematic review and meta-analysis. *Semin Arthritis Rheum* 2018; **48**: 28–34.
- 419 5 Porta S, Otero-Losada M, Kölliker Frers RA, Cosentino V, Kerzberg E, Capani F.  
420 Adipokines, Cardiovascular Risk, and Therapeutic Management in Obesity and Psoriatic  
421 Arthritis. *Front Immunol* 2021; **11**. DOI:10.3389/fimmu.2020.590749.
- 422 6 Gossec L, Smolen JS, Ramiro S, *et al*. European League Against Rheumatism (EULAR)  
423 recommendations for the management of psoriatic arthritis with pharmacological therapies:  
424 2015 update. *Annals of the Rheumatic Diseases* 2016; **75**: 499–510.
- 425 7 Gossec L, Baraliakos X, Kerschbaumer A, *et al*. EULAR recommendations for the  
426 management of psoriatic arthritis with pharmacological therapies: 2019 update. *Annals of*  
427 *the Rheumatic Diseases* 2020; **79**: 700–12.
- 428 8 Gupta S, Syrimi Z, Hughes DM, Zhao SS. Comorbidities in psoriatic arthritis: a systematic  
429 review and meta-analysis. *Rheumatol Int* 2021; **41**: 275–84.

- 1  
2 430 9 Bhole VM, Choi HK, Burns LC, *et al.* Differences in body mass index among individuals  
3 431 with PsA, psoriasis, RA and the general population. *Rheumatology* 2012; **51**: 552–6.  
4  
5 432 10 Eder L, Thavaneswaran A, Chandran V, Cook RJ, Gladman DD. Obesity is associated with  
6 433 a lower probability of achieving sustained minimal disease activity state among patients with  
7 434 psoriatic arthritis. *Ann Rheum Dis* 2015; **74**: 813–7.  
8  
9 435 11 Eder L, Abji F, Rosen CF, Chandran V, Gladman DD. The Association Between Obesity  
10 436 and Clinical Features of Psoriatic Arthritis: A Case-control Study. *J Rheumatol* 2017; **44**:  
11 437 437–43.  
12  
13 438 12 Vallejo-Yagüe E, Burkard T, Möller B, Finckh A, Burden AM. Comparison of Psoriatic  
14 439 Arthritis and Rheumatoid Arthritis Patients across Body Mass Index Categories in  
15 440 Switzerland. *Journal of Clinical Medicine* 2021; **10**: 3194.  
16  
17 441 13 di Minno MND, Peluso R, Iervolino S, *et al.* Obesity and the prediction of minimal disease  
18 442 activity: a prospective study in psoriatic arthritis. *Arthritis Care Res (Hoboken)* 2013; **65**:  
19 443 141–7.  
20  
21 444 14 Lupoli R, Pizzicato P, Scalera A, *et al.* Impact of body weight on the achievement of minimal  
22 445 disease activity in patients with rheumatic diseases: a systematic review and meta-analysis.  
23 446 *Arthritis Res Ther* 2016; **18**: 297.  
24  
25 447 15 Højgaard P, Grintborg B, Kristensen LE, Gudbjornsson B, Love TJ, Dreyer L. The influence  
26 448 of obesity on response to tumour necrosis factor- $\alpha$  inhibitors in psoriatic arthritis: results  
27 449 from the DANBIO and ICEBIO registries. *Rheumatology* 2016; **55**: 2191–9.  
28  
29 450 16 Singh S, Facciorusso A, Singh AG, *et al.* Obesity and response to anti-tumor necrosis factor-  
30 451  $\alpha$  agents in patients with select immune-mediated inflammatory diseases: A systematic  
31 452 review and meta-analysis. *PLoS One* 2018; **13**: e0195123.  
32  
33 453 17 Versini M, Jeandel P-Y, Rosenthal E, Shoenfeld Y. Obesity in autoimmune diseases: Not a  
34 454 passive bystander. *Autoimmunity Reviews* 2014; **13**: 981–1000.  
35  
36 455 18 Russolillo A, Iervolino S, Peluso R, *et al.* Obesity and psoriatic arthritis: from pathogenesis  
37 456 to clinical outcome and management. *Rheumatology* 2013; **52**: 62–7.  
38  
39 457 19 Neumann E, Hasseli R, Ohl S, Lange U, Frommer KW, Müller-Ladner U. Adipokines and  
40 458 Autoimmunity in Inflammatory Arthritis. *Cells* 2021; **10**. DOI:10.3390/cells10020216.  
41  
42 459 20 Minno MNDD, Peluso R, Iervolino S, *et al.* Weight loss and achievement of minimal disease  
43 460 activity in patients with psoriatic arthritis starting treatment with tumour necrosis factor  $\alpha$   
44 461 blockers. *Annals of the Rheumatic Diseases* 2014; **73**: 1157–62.  
45  
46 462 21 Costa L, Caso F, Ramonda R, *et al.* Metabolic syndrome and its relationship with the  
47 463 achievement of minimal disease activity state in psoriatic arthritis patients: an observational  
48 464 study. *Immunol Res* 2015; **61**: 147–53.  
49  
50 465 22 Die SCQM Foundation (Swiss Clinical Quality Management in Rheumatic Diseases).  
51 466 <https://www.scqm.ch/en/ueber-uns/> (accessed May 18, 2021).  
52  
53 467 23 Coates LC, Strand V, Wilson H, *et al.* Measurement properties of the minimal disease  
54 468 activity criteria for psoriatic arthritis. *RMD Open* 2019; **5**. DOI:10.1136/rmdopen-2019-  
55 469 001002.

- 1  
2 470 24Buuren S van, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained  
3 471 Equations in R. *Journal of Statistical Software* 2011; **45**: 1–67.  
4
- 5 472 25R Core Team (2020). R: A language and environmental for statistical computing. R  
6 473 Foundation for Statistical Computing, Vienna, Austria. <https://www.r-project.org/>  
7 474 (accessed May 14, 2021).  
8
- 9  
10 475 26Iannone F, Fanizzi R, Scioscia C, Anelli MG, Lapadula G. Body mass does not affect the  
11 476 remission of psoriatic arthritis patients on anti-TNF- $\alpha$  therapy. *Scandinavian Journal of*  
12 477 *Rheumatology* 2013; **42**: 41–4.  
13
- 14 478 27Coates LC, Orbai A-M, Morita A, *et al.* Achieving minimal disease activity in psoriatic  
15 479 arthritis predicts meaningful improvements in patients' health-related quality of life and  
16 480 productivity. *BMC Rheumatology* 2018; **2**: 24.  
17
- 18  
19 481 28McGagh D, Coates LC. Assessment of the many faces of PsA: single and composite  
20 482 measures in PsA clinical trials. *Rheumatology* 2020; **59**: i29–36.  
21
- 22 483 29Yudkin JS, Stehouwer CDA, Emeis JJ, Coppack SW. C-Reactive Protein in Healthy  
23 484 Subjects: Associations With Obesity, Insulin Resistance, and Endothelial Dysfunction.  
24 485 *Arteriosclerosis, Thrombosis, and Vascular Biology* 1999; **19**: 972–8.  
25
- 26 486 30Hak AE, Stehouwer CDA, Bots ML, *et al.* Associations of C-Reactive Protein With  
27 487 Measures of Obesity, Insulin Resistance, and Subclinical Atherosclerosis in Healthy,  
28 488 Middle-Aged Women. *Arteriosclerosis, Thrombosis, and Vascular Biology* 1999; **19**: 1986–  
29 489 91.  
30
- 31  
32 490 31Visser M. Elevated C-Reactive Protein Levels in Overweight and Obese Adults. *JAMA*  
33 491 1999; **282**: 2131.  
34
- 35 492 32Sharma S, Eckert D, Hyams JS, *et al.* Pharmacokinetics and exposure-efficacy relationship  
36 493 of adalimumab in pediatric patients with moderate to severe Crohn's disease: results from a  
37 494 randomized, multicenter, phase-3 study. *Inflamm Bowel Dis* 2015; **21**: 783–92.  
38
- 39  
40 495 33Fasanmade AA, Adedokun OJ, Ford J, *et al.* Population pharmacokinetic analysis of  
41 496 infliximab in patients with ulcerative colitis. *Eur J Clin Pharmacol* 2009; **65**: 1211–28.  
42
- 43 497 34Ternant D, Aubourg A, Magdelaine-Beuzelin C, *et al.* Infliximab pharmacokinetics in  
44 498 inflammatory bowel disease patients. *Ther Drug Monit* 2008; **30**: 523–9.  
45
- 46 499 35Versini M, Jeandel P-Y, Rosenthal E, Shoenfeld Y. Obesity in autoimmune diseases: not a  
47 500 passive bystander. *Autoimmun Rev* 2014; **13**: 981–1000.  
48
- 49  
50 501 36Statistik B für Übergewicht und Adipositas - Schweizerische Gesundheitsbefragung 2017 |  
51 502 Publikation. Bundesamt für Statistik. 2020; published online Sept 3.  
52 503 <https://www.bfs.admin.ch/asset/de/14147705> (accessed June 5, 2022).  
53
- 54 504 37Gulfe A, Geborek P, Saxne T. Response criteria for rheumatoid arthritis in clinical practice:  
55 505 how useful are they? *Ann Rheum Dis* 2005; **64**: 1186–9.  
56
- 57 506 38Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis:  
58 507 a proposed objective target for treatment. *Ann Rheum Dis* 2010; **69**: 48–53.  
59  
60

- 1  
2 508 39 Body mass index - BMI. [https://www.euro.who.int/en/health-topics/disease-](https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi)  
3 509 [prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi](https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi) (accessed June 23, 2021).  
4  
5 510 40 Obesity and overweight. [https://www.who.int/news-room/fact-sheets/detail/obesity-and-](https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight)  
6 511 [overweight](https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight) (accessed July 8, 2021).  
7  
8 512 41 Lee Y, Kwan Y, Lim K, *et al.* A systematic review of the association of obesity with the  
9 513 outcomes of inflammatory rheumatic diseases. *smelj* 2019; **60**: 270–80.  
10  
11 514 42 Queiro R. Cardiometabolic comorbidity in the selection of treatment in spondyloarthritis:  
12 515 one step closer to truly personalized medicine? *Expert Opin Biol Ther* 2021; **21**: 1539–41.  
13  
14  
15 516  
16 517  
17 518  
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For peer review only

1  
2 520 **FIGURE LEGENDS**  
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7 522 (Attached as JPG)

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9 523 **Figure 1.** Results from the multivariable logistic regression investigating the association  
10  
11 524 between body mass index (BMI) categories and various clinical outcomes. Maximum follow-  
12  
13 525 up 12-months.  
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23 529 **Figure 2.** Distribution of patients achieving the study primary and secondary outcomes within  
24  
25 530 the first year, and percentage of patients achieving treatment persistence at the end of month-  
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27 531 12, stratified by body mass index (BMI) category. Abbreviations: MDA Minimal Disease  
28  
29 532 Activity; DAPSRem Disease Activity for Psoriatic Arthritis (DAPSA) remission;  
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31 533 DAPSRemLDA DAPSA remission or low disease activity; cDAPSRem clinical DAPSA  
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33 534 remission; DAS28rem 28-joint disease activity score remission.  
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41 537 (Attached as JPG)

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43 538 **Figure 3.** Venn Diagram depicting the number of patients (counts) achieving the study  
44  
45 539 individual primary and secondary outcomes within the first year, overall and stratifying by  
46  
47 540 body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSRem  
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49 541 Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSRemLDA DAPSA  
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51 542 remission or low disease activity; cDAPSRem clinical DAPSA remission; DAS28rem 28-  
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53 543 joint disease activity score remission.  
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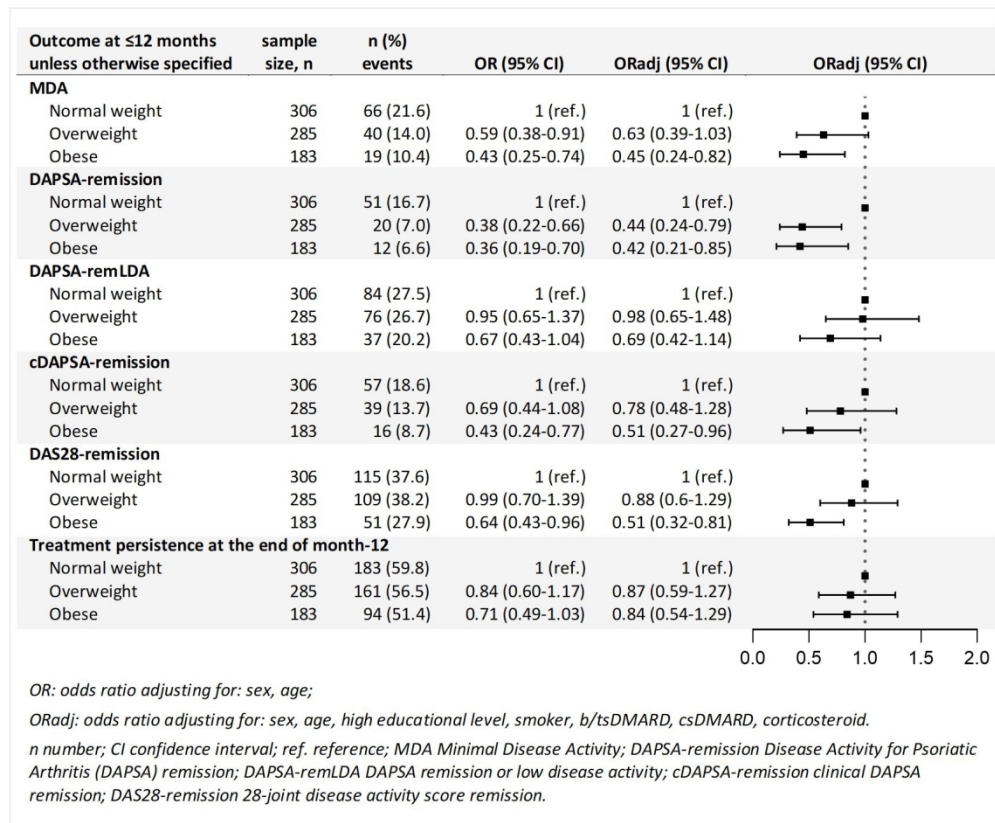


Figure 1. Results from the multivariable logistic regression investigating the association between body mass index (BMI) categories and various clinical outcomes. Maximum follow-up 12-months.

301x249mm (144 x 144 DPI)

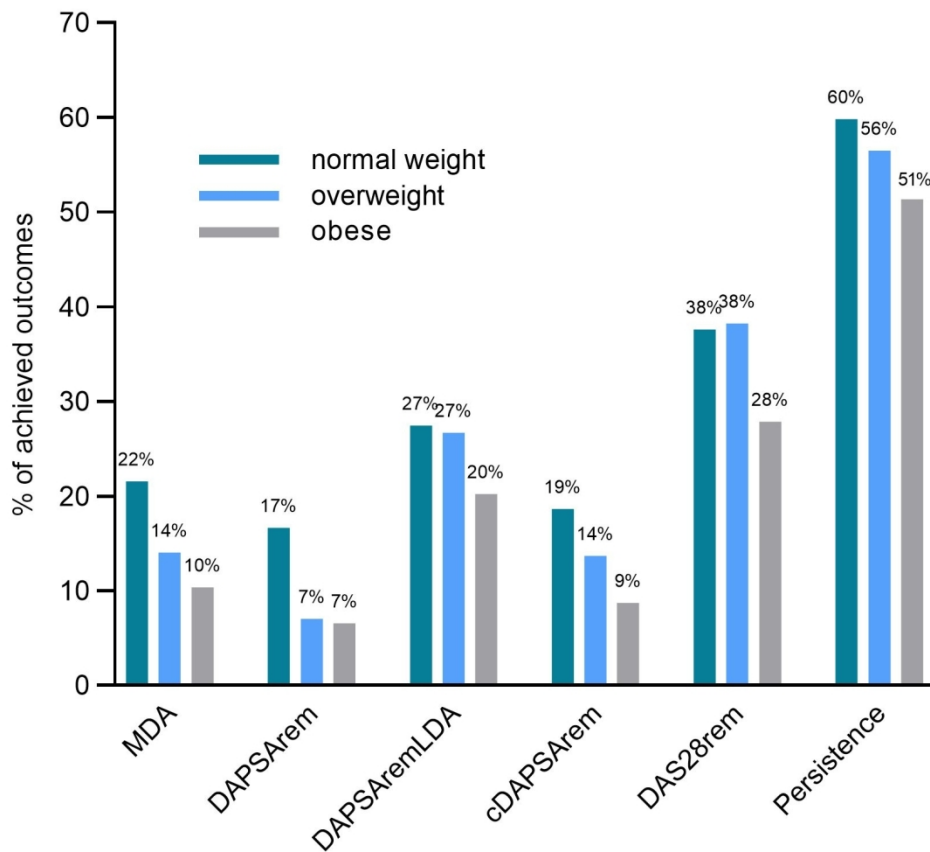


Figure 2. Distribution of patients achieving the study primary and secondary outcomes within the first year, and percentage of patients achieving treatment persistence at the end of month-12, stratified by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSAreM Disease Activity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

306x275mm (144 x 144 DPI)



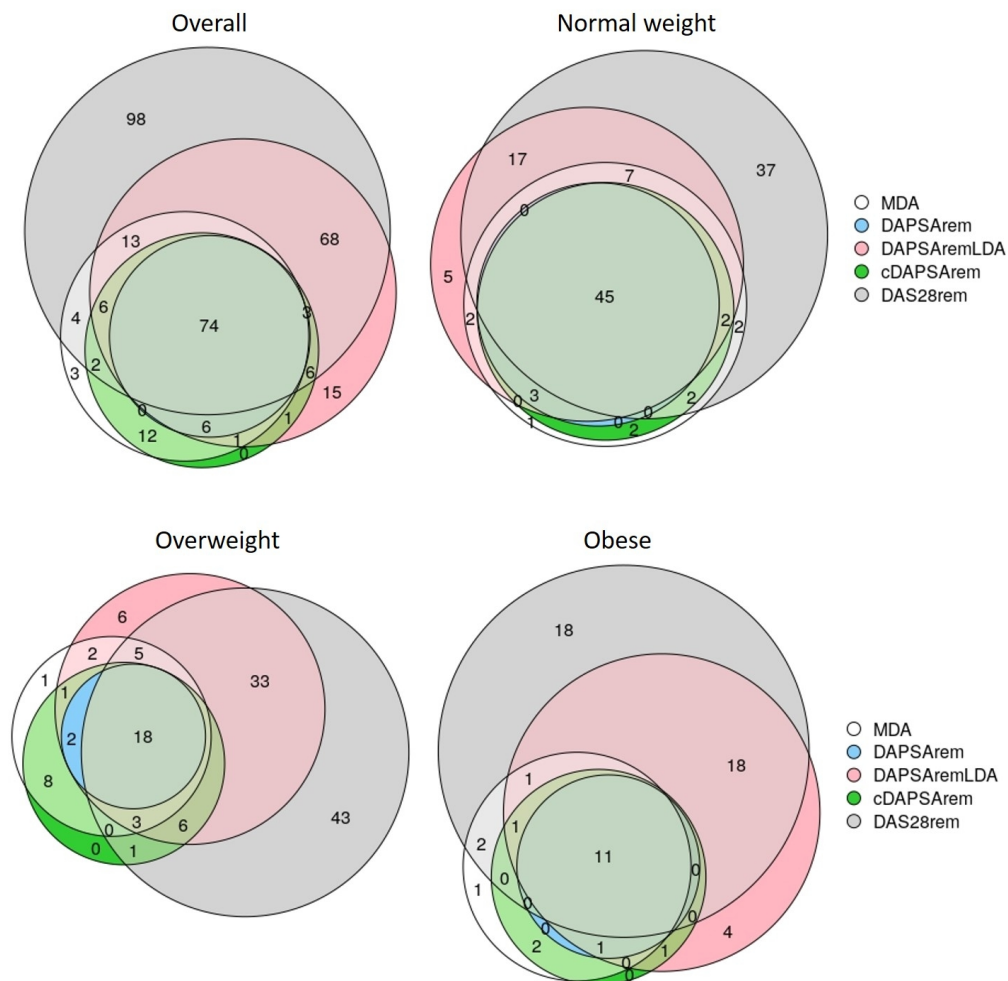


Figure 3. Venn Diagram depicting the number of patients (counts) achieving the study individual primary and secondary outcomes within the first year, overall and stratifying by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis (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

# 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

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

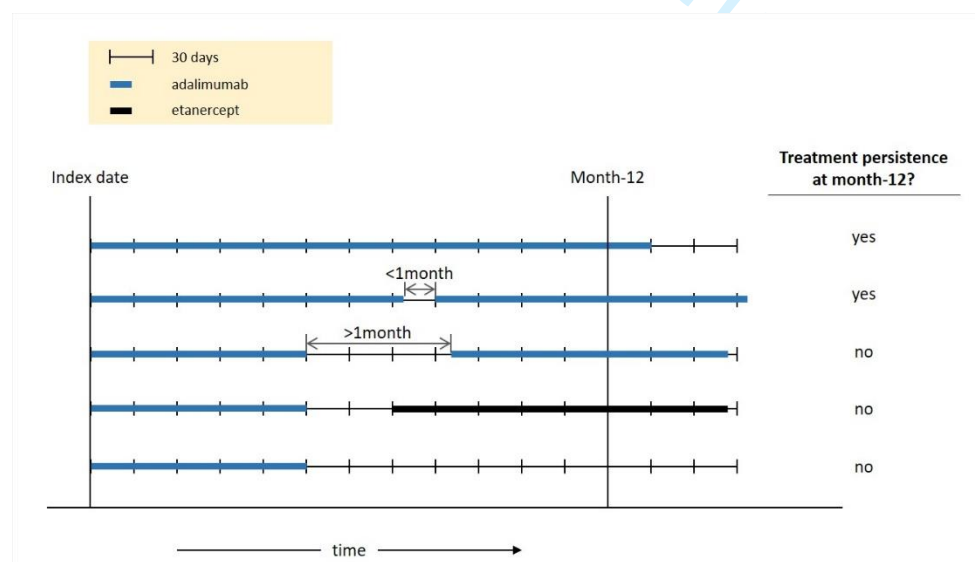
$$(2) \text{ DAPSA} = \text{sjc66} + \text{tjc68} + \text{PatActivity} + \text{PatPain} + \text{CRP}$$

$$(3) \text{ cDAPSA} = \text{sjc66} + \text{tjc68} + \text{PatActivity} + \text{PatPain}$$

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

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

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



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

**Supplementary Table S1.** Variables included in the multiple imputation.

| Variable   | Version 1 Included | Version 2 Included | Predicted | Predictor        | Method                          | Missingness | Levels   | Range         |
|--|--------------------|--------------------|-----------|------------------|---------------------------------|-------------|--|---------------|
| Outcome <sup>a</sup><br>(MDA/DAPSArem/DAPSAremLDA/Persistence) | yes                | -                  | -         | yes              | -                               | -           | yes; no.   | -             |
| Outcome <sup>a</sup> (DAS28rem)                                | -                  | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Patient ID   | yes                | yes                | -         | -                | -                               | -           | -  | 1-774         |
| BMI category   | yes                | yes                | -         | -                | -                               | -           | normal weight;<br>overweight;<br>obese.  | -             |
| BMI kg/m <sup>2</sup>  | yes                | yes                | -         | yes              | -                               | -           | -  | 16.56 - 51.42 |
| Sex  | yes                | yes                | -         | yes              | -                               | -           | female (women);<br>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;<br>almost none;<br>mild;<br>mild to moderate;<br>moderate;<br>moderate to severe;<br>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 <sup>b</sup> | passive imputation <sup>d</sup> | 298 (38.5)  | -  | 0.10 - 121    |
| DAS28  | -                  | yes                | yes       | yes <sup>c</sup> | passive imputation <sup>e</sup> | 99 (12.79)  | -  | 0.20 - 7.60   |
| HAQ (0-3)  | yes                | yes                | yes       | yes              | pmm                             | 167 (21.58) | -  | 0 - 3         |
| SF-12mcs (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;<br>other biologic;<br>tsDMARD.  | -             |
| csDMARD at index   | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Prednisone at index  | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Dactylitis   | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Sacroiliitis   | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Enthesitis   | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Spinal involvement   | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Coxitis  | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Dactylitis   | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |

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

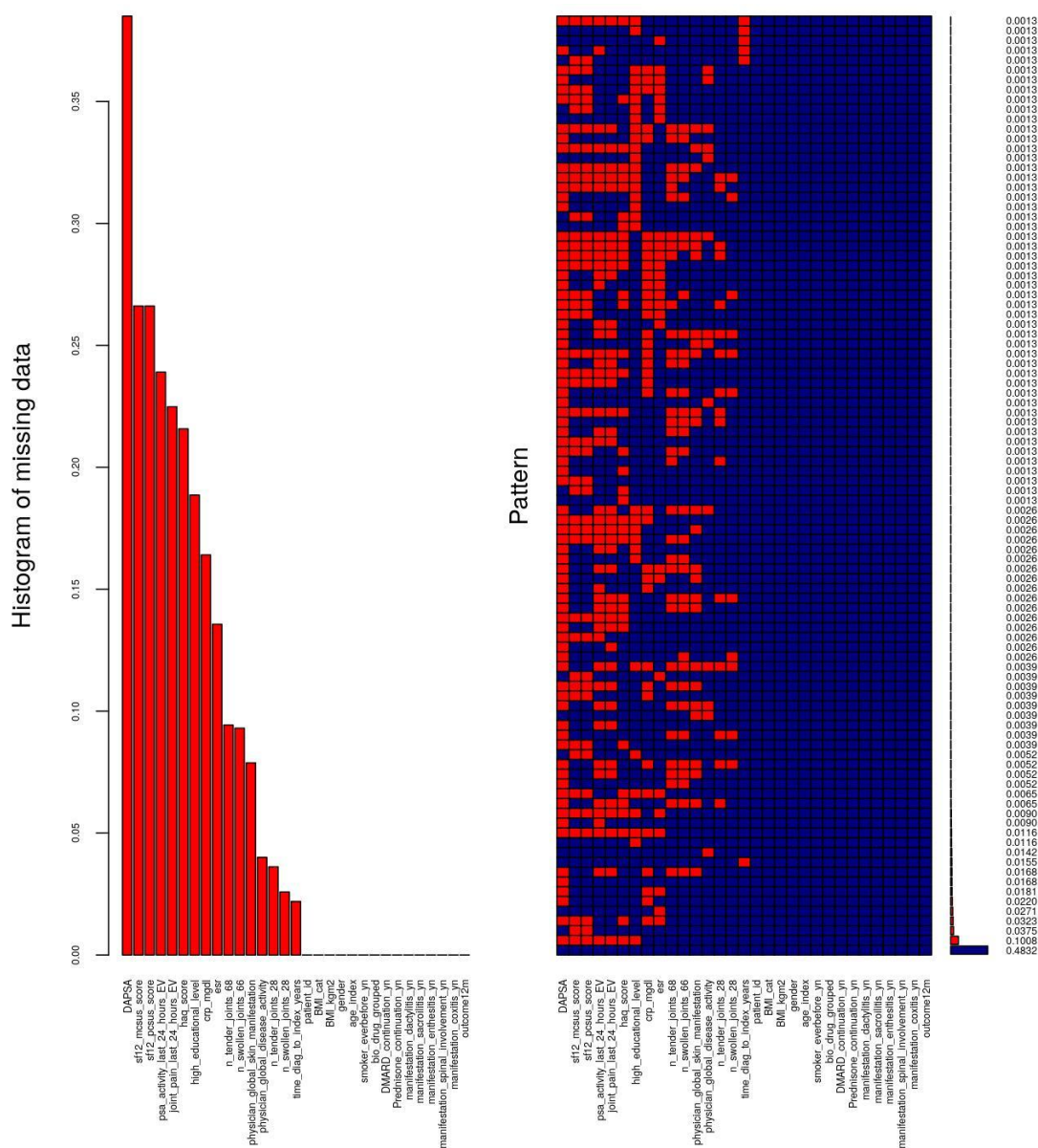
<sup>a</sup> Multiple imputation was run distinctly for each outcome.

<sup>b</sup> DAPSA not used as predictor for: sjc66, tjc68, PatActivity, PatPain, CRP.

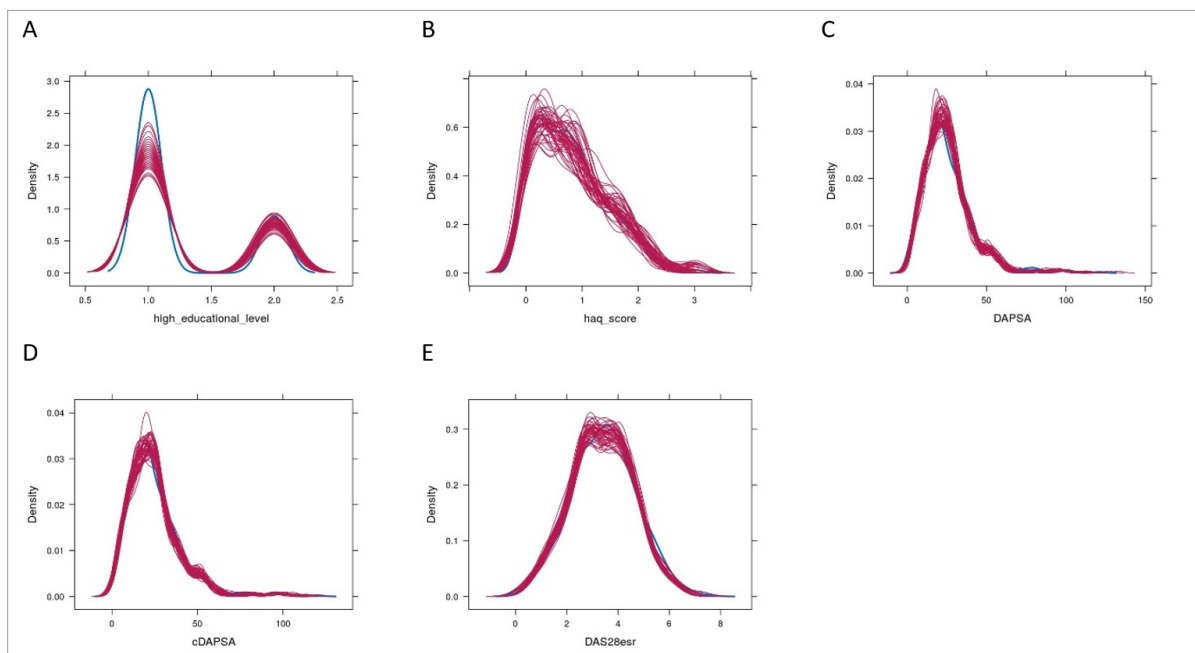
<sup>c</sup> DAS28 not used as predictor for: sjc28, tjc28, ESR.

<sup>d</sup> DAPSA passive imputation:  $DAPSA = sjc66 + tjc68 + PatActivity + PatPain + CRP$

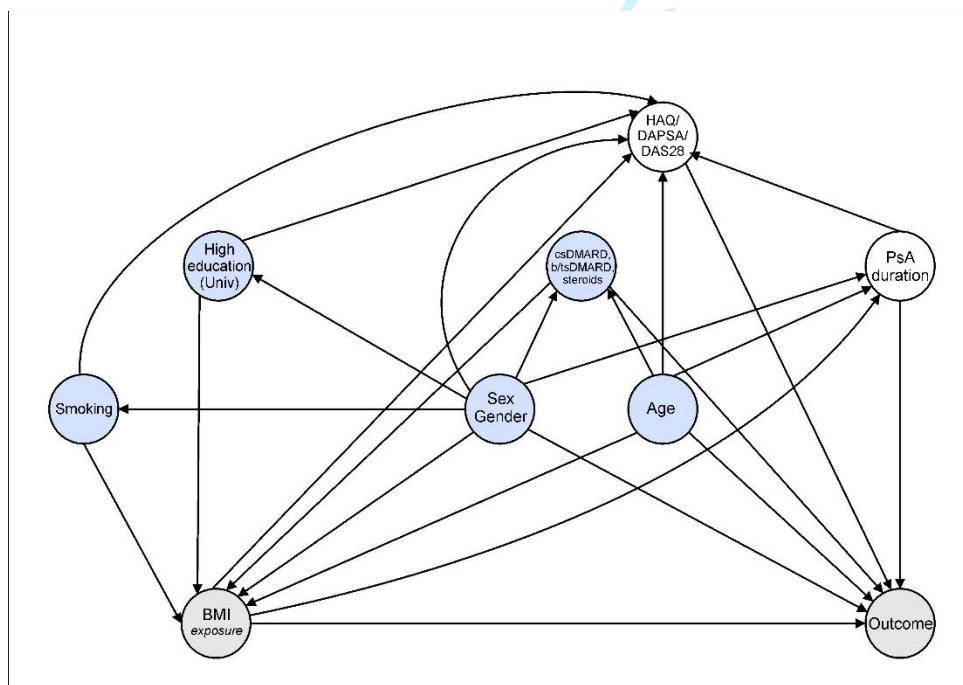
<sup>e</sup> DAS28 passive imputation:  $DAS28ESR = (0.56 \times \sqrt{tjc28} + 0.28 \times \sqrt{sjc28} + 0.7 \times \ln(ESR)) \times 1.08 + 0.16$



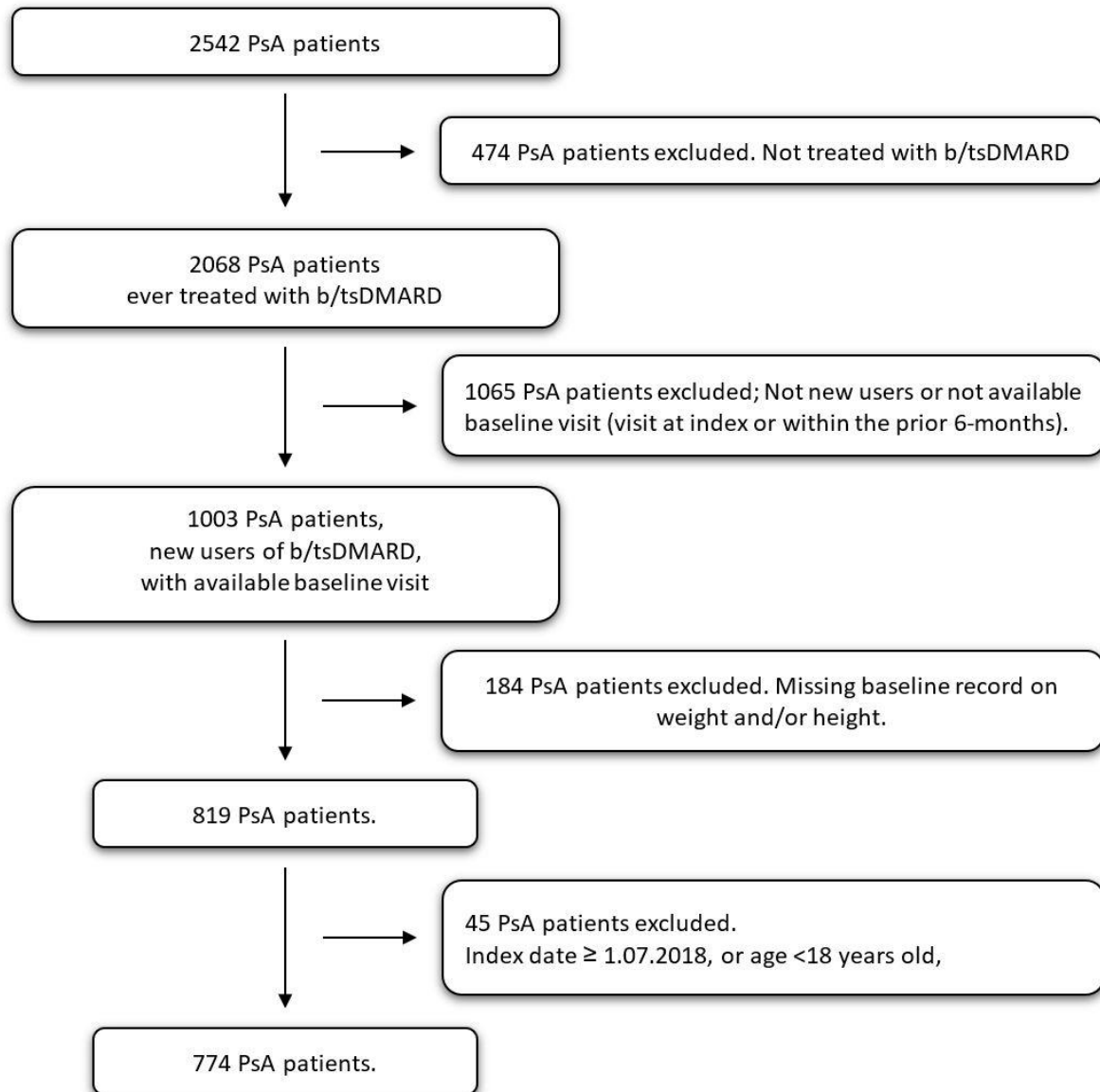
**Supplementary Figure S2.** Graphical representation of the missingness among baseline variables included in the imputations for primary analysis (i.e., achievement of Minimal Disease Activity (MDA) within the first year after index date). The 48.32% of patients had complete information on all the included 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 rationale 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 <sup>c</sup> (95% CI) | n events                    | ORadj <sup>c</sup> (95% CI) | n events                    | ORadj <sup>c</sup> (95% CI) |
| <b>MDA</b>                   |               |                            |                             |                             |                             |                             |                             |
| 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)             |
| <b>DAPSA-remission</b>       |               |                            |                             |                             |                             |                             |                             |
| 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)               |
| <b>DAPSA-remLDA</b>          |               |                            |                             |                             |                             |                             |                             |
| 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)            |
| <b>cDAPSA-remission</b>      |               |                            |                             |                             |                             |                             |                             |
| 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)             |
| <b>DAS28-remission</b>       |               |                            |                             |                             |                             |                             |                             |
| 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)            |
| <b>Treatment persistence</b> |               |                            |                             |                             |                             |                             |                             |
| Normal weight                | 306           | 204 (66.7)                 | 1 (ref.)                    | 183 (59.8)                  | 1 (ref.)                    | 159 (52.0)                  | 1 (ref.)                    |
| Overweight                   | 285           | 184 (64.6)                 | 0.92 (0.61-1.4)             | 161 (56.5)                  | 0.88 (0.59-1.3)             | 148 (51.9)                  | 1.04 (0.71-1.54)            |
| Obese                        | 183           | 111 (60.7)                 | 0.92 (0.56-1.49)            | 94 (51.4)                   | 0.92 (0.58-1.46)            | 81 (44.3)                   | 1.04 (0.66-1.64)            |

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

Abbreviations: n number; CI confidence interval; ref. reference; 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 <sup>a</sup> (95% CI) | ORadj <sup>b</sup> (95% CI) | ORadj <sup>c</sup> (95% CI) |
| <b>MDA</b>              |   |            |                          |                             |                             |
| 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)            |
| <b>DAPSA-remission</b>  |   |            |                          |                             |                             |
| 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)            |
| <b>DAPSA-remLDA</b>     |   |            |                          |                             |                             |
| 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)            |
| <b>cDAPSA-remission</b> |   |            |                          |                             |                             |
| 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)            |
| <b>DAS28-remission</b>  |   |            |                          |                             |                             |
| Normal weight           | 159   | 115 (72.3) | 1 (ref.)                 | 1 (ref.)                    | 1 (ref.)                    |
| Overweight              | 153   | 109 (71.2) | 0.86 (0.51-1.46)         | 0.55 (0.3-1.01)             | 0.57 (0.28-1.14)            |
| Obese                   | 89  | 51 (57.3)  | 0.48 (0.27-0.86)         | 0.3 (0.15-0.6)              | 0.37 (0.17-0.81)            |

OR: odds ratio adjusting for: sex, age;

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

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

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



**Supplementary Table S4.** Sensitivity analyses, excluding the 12 patients with body mass index (BMI) <18.5 kg/m<sup>2</sup>. 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<br>(Excluding BMI<18.5)         | n<br>sample size | Maximum follow-up 12-months |                  |                  |
|--|------------------|-----------------------------|------------------|------------------|
|  |                  | n<br>vents                  | OR               | ORadj            |
| <b>MDA</b>   |                  |                             |                  |                  |
| 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) |
| <b>DAPSA-remission</b>                               |                  |                             |                  |                  |
| 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) |
| <b>DAPSA-remLDA</b>                                  |                  |                             |                  |                  |
| 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) |
| <b>cDAPSA-remission</b>                              |                  |                             |                  |                  |
| 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) |
| <b>DAS28-remission</b>                               |                  |                             |                  |                  |
| 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) |
| <b>Treatment persistence at the end of follow-up</b> |                  |                             |                  |                  |
| 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 |          |             |           |          | Overall<br>(n=774)<br>(counts) | Normal weight<br>(n=306)<br>(counts) | Overweight<br>(n=285)<br>(counts) | Obese<br>(n=183)<br>(counts) |
|-------------------|----------|-------------|-----------|----------|--------------------------------|--------------------------------------|-----------------------------------|------------------------------|
| MDA               | DAPSArem | DAPSAremLDA | cDAPSArem | DAS28rem |                                |                                      |                                   |                              |
| ✓                 | -        | -           | -         | -        | 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**Enriqueta Vallejo-Yagüe<sup>1</sup>, Theresa Burkard<sup>1</sup>, Andrea M. Burden<sup>1</sup><sup>1</sup> Department of Chemistry and Applied Biosciences, Institute of Pharmaceutical Sciences, ETH Zurich, Zurich, Switzerland.STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

|                              | Item No | Recommendation   | Page No                               |
|------------------------------|---------|--|---------------------------------------|
| <b>Title and abstract</b>    | 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                                     |
| <b>Introduction</b>          |         |  |                                       |
| 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                                     |
| <b>Methods</b>               |         |  |                                       |
| 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/<br>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;<br>Supplementary<br>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                                   |

|                          |     |   |   |
|--------------------------|-----|---|---|
| <b>Results</b>           |     |   |   |
| 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<br>(b) Give reasons for non-participation at each stage<br>(c) Consider use of a flow diagram   | Supplementary Figure S5<br><br>Supplementary Figure S5<br>Supplementary Figure S5 |
| Descriptive data         | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate number of participants with missing data for each variable of interest<br>(c) Summarise follow-up time (eg, average and total amount)  | 9<br><br>Table 1<br><br>NA (see page 7)   |
| Outcome data             | 15* | Report numbers of outcome events or summary measures over time  | Figure 1;<br>Table 2;<br>Figure 2;<br>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<br>(b) Report category boundaries when continuous variables were categorized<br>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 11-12;<br>Figure 1;<br>Table 2<br><br>6-7 (exposure and outcome)<br>-             |
| Other analyses           | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses  | 12-13   |
| <b>Discussion</b>        |     |   |   |
| 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   | -   |
| <b>Other information</b> |     |   |   |
| 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>.

# BMJ Open

## 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

|                                 |  |
|---------------------------------|--|
| Journal:                        | <i>BMJ Open</i>  |
| Manuscript ID                   | bmjopen-2022-061474.R2   |
| Article Type:                   | Original research  |
| Date Submitted by the Author:   | 18-Aug-2022  |
| Complete List of Authors:       | Vallejo-Yagüe, Enriqueta; ETH Zürich, Institute of Pharmaceutical Sciences, Department of Chemistry and Applied Biosciences<br>Burkard, Theresa; ETH Zürich, Institute of Pharmaceutical Sciences, Department of Chemistry and Applied Biosciences<br>Micheroli, Raphael; University Hospital of Zurich, University of Zurich, Department of Rheumatology<br>Burden, Andrea; ETH Zurich, Institute of Pharmaceutical Sciences, Department of Chemistry and Applied Biosciences |
| <b>Primary Subject Heading</b>: | Rheumatology   |
| Secondary Subject Heading:      | Epidemiology   |
| Keywords:                       | RHEUMATOLOGY, EPIDEMIOLOGY, Rheumatology < INTERNAL MEDICINE   |
|                                 |  |

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3 1 **Minimal Disease Activity and remission in psoriatic arthritis**  
4 **patients with elevated body mass index: an observational cohort**  
5 **study in the Swiss Clinical Quality Management cohort**  
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34 24 **Keywords:** psoriatic arthritis; minimal disease activity; remission; obesity; body mass index.  
35  
36  
37 25  
38  
39 26 Abstract word count: 293  
40  
41 27 Manuscript word count: 3530  
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## 30 ABSTRACT

31 **Objective:** To assess the impact of elevated body mass index (BMI) in the achievement of  
32 Minimal Disease Activity (MDA) and several definitions of remission in PsA patients in  
33 Switzerland. Secondly, to assess the overlapping across the study outcomes.

34 **Methods:** This observational cohort study in the Swiss Clinical Quality Management in  
35 Rheumatic Diseases (SCQM) registry included PsA patients starting their first biologic or  
36 targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) from 1997 to  
37 30.06.2018. Exposure was BMI category at b/tsDMARD start: overweight, obese, and normal  
38 weight (reference). Logistic regression was used to assess the achievement of MDA and  
39 remission at  $\leq 12$ -months, as well as treatment persistence at one-year, in overweight and obese  
40 patients compared to the normal weight group. Remission was defined by Disease Activity for  
41 Psoriatic Arthritis (DAPSA), clinical DAPSA (cDAPSA), and 28-joint disease activity score  
42 (DAS28). Additionally, overlapping across study outcomes was investigated.

43 **Results:** The study included 306 (39.5%) normal weight, 285 (36.8%) overweight, and 183  
44 (23.6%) obese patients. Compared to the normal weight group, obese patients had lower odds  
45 of achieving MDA at  $\leq 12$ -months (Adjusted odds ratio [OR<sub>adj</sub>] 0.45, 95% confidence interval  
46 [CI] 0.24-0.82). This was consistent with the observed reduced odds of achieving DAPSA-  
47 remission (OR<sub>adj</sub> 0.42, 95%CI 0.21-0.85), cDAPSA-remission (OR<sub>adj</sub> 0.51, 95%CI 0.27-  
48 0.96), and DAS28-remission (OR<sub>adj</sub> 0.51, 95%CI 0.32-0.81) in obese vs normal weight  
49 patients. Among the 125 patients achieving MDA, the majority (81.8% normal weight, 80.0%  
50 overweight, 78.9% obese) achieved cDAPSA-remission. No differences were observed in the  
51 odds to achieving treatment persistence between the BMI strata.

52 **Conclusions:** Obesity halved the likelihood of achieving MDA and remission in PsA patients  
53 with b/tsDMARDs compared to those with normal weight, while it did not impact treatment  
54 persistence. High overlapping of patients achieving the outcomes MDA and cDAPSA-  
55 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.

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## 59 INTRODUCTION

60 Psoriatic arthritis (PsA) is an immune-mediated rheumatic disease,<sup>1</sup> with an estimated  
61 prevalence of 0.05-0.42%,<sup>2-4</sup> and 5-41% among patients with psoriasis.<sup>3</sup> PsA is a complex and  
62 multifactorial disease,<sup>5</sup> for which pathological features include musculoskeletal involvement,  
63 such as inflammation of the peripheral joints (arthritis), the entheses (enthesitis), the axial  
64 skeleton (spondylitis), and the finger and toe digits (dactylitis), as well as extra-articular  
65 manifestations involving skin and nails, and potentially other organs.<sup>6</sup> Pharmacological  
66 treatments include conventional synthetic disease-modifying anti-rheumatic drugs  
67 (csDMARDs) and biologic or targeted synthetic disease-modifying anti-rheumatic drugs  
68 (b/tsDMARDs).<sup>3</sup> Treatment of PsA aims to maximise health-related quality of life (QoL),  
69 through targeting symptoms and structural damage,<sup>7</sup> and it is recommended to target  
70 low/minimal disease activity or remission.<sup>6</sup>

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

78 The rationale behind the association between obesity and PsA has been previously  
79 discussed.<sup>5,17,18</sup> In short, obesity has been described as a low-grade inflammatory disease,<sup>18</sup> and  
80 both obesity and PsA share pathological inflammatory pathways.<sup>5,18,19</sup> Further evidence  
81 supporting the association between obesity and a worse PsA clinical outcome is the association  
82 of weight loss with higher rate of achieving MDA.<sup>20</sup> Additionally, obesity is a well-known  
83 contributor to the metabolic syndrome (MetS), and MetS was similarly associated to lower  
84 likelihood of achieving MDA in PsA patients.<sup>21</sup>

1  
2 85 Despite the growing evidence on the association between obesity and worse clinical  
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4 86 response in PsA patients, most published observational cohort studies on this topic had  
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6 87 relatively small sample size. For example, a systematic review investigating the association  
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8 88 between obesity and response in immune-mediated inflammatory diseases identified one  
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10 89 randomised clinical trial and eight observational cohort studies in PsA patients, but six of the  
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12 90 included observational cohorts had a sample size  $\leq 330$ .<sup>16</sup> Thus, further investigating this effect,  
13  
14 91 especially in a different and bigger population cohort, remains of interest. Additionally, it is  
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16 92 unclear whether the findings would remain consistent across outcome definitions.  
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20 93 Thus, we seek to contribute to the growing body of evidence by performing an  
21  
22 94 observational cohort study aiming to assess the impact of BMI in the achievement of MDA and  
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24 95 remission in PsA patients. Additionally, by including several outcome definitions we aim to  
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26 96 investigate the consistency of the findings when considering different aspects of the disease.  
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## 30 97 **METHODS**

### 31 98 **Study design and data source**

32  
33 99 We performed an observational cohort study in the Swiss Clinical Quality Management in  
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35 100 Rheumatic Diseases (SCQM) registry from January 1<sup>st</sup> 1997 and July 31<sup>st</sup> 2019. The SCQM is  
36  
37 101 a national longitudinal population-based cohort of rheumatic diseases in Switzerland, initiated  
38  
39 102 in 1997.<sup>22</sup> SCQM data are recorded during routine clinical practice, and includes information  
40  
41 103 on demographics, body height and weight, life-style habits, anti-rheumatic medication (with  
42  
43 104 start and stop dates), clinical endpoints, patient-reported outcomes, and health standardized  
44  
45 105 surveys.<sup>12,22</sup> Diagnosis of PsA is recorded in SCQM following the physician's criteria.  
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### 50 106 **Study population**

51  
52 107 PsA patients ( $\geq 18$  years old) starting their first b/tsDMARD in the SCQM registry between  
53  
54 108 June 1<sup>st</sup> 2020 and June 30<sup>th</sup> 2018 (inclusive) were included in the study. The first recorded start  
55  
56 109 of b/tsDMARD in the SCQM was defined as the index date. Patients with a b/tsDMARD start  
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1  
2 110 date before their first registered visit at SCQM were excluded. Similarly, patients without a  
3  
4 111 baseline record on height and weight were excluded.

## 6 112 **Exposure**

8  
9 113 The exposure of interest was BMI category at the start of the patients' first b/tsDMARD.  
10  
11 114 Baseline BMI ( $\text{kg}/\text{m}^2$ ) was calculated using height and weight records (**Supplementary**  
12  
13 115 **Equation 1**) at index date or as close as possible to this date within a 6-month look-back  
14  
15 116 window. Measures of height and weight are taken in the clinic, during routine visits to the  
16  
17 117 rheumatologist. Patients were classified based on BMI as normal weight (BMI  $<25$ ),  
18  
19 118 overweight (BMI 25.0-29.9), and obese (BMI  $\geq 30$ ). The normal weight group was the reference  
20  
21 119 category.

## 24 120 **Outcomes**

26  
27 121 The primary outcome was defined as achievement of MDA within the first year after the index  
28  
29 122 date. MDA was achieved if at least five of the following seven criteria were met: number of  
30  
31 123 tender joint counts (TJC)  $\leq 1$ ; number of swollen joint counts (SJC)  $\leq 1$ ; skin manifestation none  
32  
33 124 or almost none; patient's joint pain by visual analogue scale (VAS, 0-100)  $\leq 15$ ; patient's  
34  
35 125 assessment on PsA activity by VAS  $\leq 20$ ; Health Assessment Questionnaire (HAQ)  $\leq 0.5$ ;  
36  
37 126 enthesitis points  $\leq 1$ .<sup>23</sup>

38  
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41 127 Secondary outcomes assessed within the first year were: achievement of Disease  
42  
43 128 Activity for Psoriatic Arthritis (DAPSA) remission, defined as DAPSA  $\leq 4$ ; DAPSA remission  
44  
45 129 or low disease activity (DAPSA-remLDA), defined as DAPSA  $\leq 14$ ; clinical DAPSA  
46  
47 130 (cDAPSA) remission, defined as cDAPSA  $\leq 4$ ; and 28-joint disease activity score (DAS28)  
48  
49 131 remission, defined as DAS28  $< 2.6$ . DAPSA, cDAPSA, and DAS28 formulas are described in  
50  
51 132 the **Supplementary Equations 2-5**. DAS28-remission was calculated using erythrocyte  
52  
53 133 sedimentation rate (ESR; DAS28-ESR), however, in cases where follow-up data on DAS28-  
54  
55 134 ESR was missing, DAS28 with C-reactive protein (CRP; DAS28-CRP) was used instead, if  
56  
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58  
59 135 available.

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2 136 As a tertiary outcome, persistence with the first b/tsDMARD at the end of month-12 was  
3  
4 137 assessed. We allowed for a permissible gap of one-month between treatment courses of the  
5  
6 138 same b/tsDMARD, as illustrated in the **Supplementary Figure S1**.

8  
9 139 Patients with missing information on the study outcomes during the follow-up were  
10  
11 140 categorized as not having achieved the corresponding outcome. In a sensitivity analysis, we re-  
12  
13 141 ran our analyses excluding patients with missing information on outcome during follow-up.

#### 142 **Follow-up**

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

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

#### 150 **Covariates**

151 Baseline variables included demographics, BMI, high education, ever smoking, anti-rheumatic  
152 medication (i.e., b/tsDMARD, csDMARD, corticosteroid), inflammatory markers or acute  
153 phase reactants (i.e., ESR, CRP), physician's assessment on disease activity and skin, patient-  
154 reported disease activity and pain, tender and swollen joint counts (counting 28 joints),  
155 composite disease activity scores (i.e., DAPSA, cDAPSA, DAS28-ESR), disease-specific  
156 manifestations (i.e., musculoskeletal manifestations, dactylitis, enthesitis, sacroilitis, spinal  
157 involvement, coxitis, peripheral arthritis, nail manifestation), health standardized surveys (i.e.,  
158 Health Assessment Questionnaire [HAQ], Short Form-12 [SF-12]), and comorbidities (i.e.,  
159 cardiovascular event/disease, diabetes or other metabolic problems, depression/anxiety).  
160 Baseline variables were collected at index date, or as close as possible to that date within a 6-  
161 month look-back window, except for: composite disease activity scores, disease-specific

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

166 Additional information on covariates is included in Supplementary Text S1.

### 167 **Data analysis**

168 Patient baseline characteristics were described, and the overweight and obese categories were  
169 compared to the normal weight group (reference group) using chi-squared test for categorical  
170 variables and t-test, ANOVA, or Kruskal-Wallis test for continuous variables. For these tests,  
171 missing values did not function as a grouping variable. Statistical significance was defined as  
172  $p \leq 0.05$ .

173 Subsequently, missingness for key baseline variables was addressed with multiple  
174 imputation by chained equation (MICE) using the *mice* package<sup>24</sup> in the R Statistical  
175 Software.<sup>25</sup> MICE was performed for each study outcome separately, using 50 imputations with  
176 15 interactions for each set. Variables included in the imputations, their original missingness,  
177 and corresponding applied imputation models are presented in the **Supplementary Table S1**.  
178 The 48.32% of the study population had complete information on every variable included in  
179 the MICE for the main analysis (**Supplementary Figure S2**). Convergence of imputations was  
180 assessed by visual inspection of density plots (**Supplementary Figure S3**).

181 To investigate the association between BMI categories and the study outcomes,  
182 multivariable logistic regression models were conducted (outcome specific) for individual  
183 imputed datasets, and the results were pooled to a single estimate according to Rubin's rules.  
184 These models were conducted first, including only sex and age as covariates, and second,  
185 adding clinical confounders (full-adjusted). Confounders were chosen based on clinical  
186 rational and direct acyclic graphs (DAGs) (**Supplementary Figure S4**), and included: sex  
187 (male; female), age, high education (yes/no), ever smoking (yes/no), b/tsDMARD (TNFi; other



1  
2 188 biologic; tsDMARD), csDMARD at index date (yes/no), and corticosteroid use at index date  
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4 189 (yes/no). Additionally, sensitivity analyses were performed whereby we added the respective  
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6 190 composite disease activity score or health standardized survey to the fully adjusted models for  
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8 191 primary and secondary outcomes to assess their potential mediating impact on the analyses.  
9  
10 192 Another sensitivity analysis addressed the one-year outcomes after excluding patients with  
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12 193 underweight (BMI<18.5 kg/m<sup>2</sup>)  
13

14  
15 194 Lastly, to compare the overlapping across study outcomes, the proportion of patients  
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17 195 achieving each outcome (per BMI group) was summarised, and the overlapping of patients  
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19 196 achieving individual primary and secondary outcomes during the first year was illustrated with  
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21 197 a Venn Diagram.  
22

### 23 198 **Patient and Public Involvement**

24  
25 199 Patients or the public were not involved in the design, or conduct, or reporting, or dissemination  
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27 200 plans of our research.  
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## 31 201 **RESULTS**

32  
33 202 The study included 774 adult PsA patients starting their first b/tsDMARD. **Supplementary**  
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35 203 **Figure S5** illustrates the cohort selection process. Among included patients, 306 (39.53%) were  
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37 204 normal weight, 285 (36.82%) were overweight, and 183 (23.64%) were obese. Baseline patient  
38  
39 205 characteristics (prior to imputation) are presented in **Table 1**. Compared to the normal weight  
40  
41 206 group, overweight patients had higher SJC, were less frequently women, and had older mean  
42  
43 207 age. Both overweight and obese patients had lower frequency of high education, and higher  
44  
45 208 patient-reported disease activity and joint pain, while only obese patients had higher CRP  
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47 209 levels. Compared to the normal weight category, DAPSA and DAS28 were elevated in the  
48  
49 210 overweight group, while cDAPSA was higher in both overweight and obese BMI categories.  
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51 211 HAQ and SF-12 with physical components (SF-12pcs) were worse in the obese patients, and  
52  
53 212 patients with obesity were more likely to have had a cardiovascular event/disease than the  
54  
55 213 normal weight group.  
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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<br>(n=306) | Overweight<br>(n=285) | p-value | Obese<br>(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/tsDMARD   |                          |                       | 0.87    |                     | 0.35    |
| TNFi biologic <sup>a</sup>                              | 279 (91.18)              | 262 (91.93)           |         | 160 (87.43)         |         |
| other biologic <sup>b</sup>                             | 9 (2.94)                 | 9 (3.16)              |         | 6 (3.28)            |         |
| tsDMARD <sup>c</sup>                                    | 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    |
| Sacroiliitis  | 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)          |         |

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|                                      |               |              |      |              |      |
|--------------------------------------|---------------|--------------|------|--------------|------|
| 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<sup>2</sup>); Overweight (BMI 25.0-29.9 kg/m<sup>2</sup>); Obese (BMI ≥30 kg/m<sup>2</sup>).

<sup>a</sup> adalimumab, etanercept, infliximab, certolizumab, golimumab; <sup>b</sup> abatacept, secukinumab, tocilizumab, ustekinumab; <sup>c</sup> 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.

217

218 Results from the logistic regression for the primary analysis are presented in **Figure 1**.

219 Compared to the normal weight group, obese patients had significantly lower odds of achieving  
 220 MDA within the first year, with an adjusted Odds Ratio (OR<sub>adj</sub>) of 0.45 (95% confidence  
 221 interval [CI] 0.24-0.82). Similarly, both overweight and obese patients had >50% reduced odds  
 222 of achieving DAPSA-remission (overweight OR<sub>adj</sub> 0.44 [95% CI 0.24-0.79] and obese OR<sub>adj</sub>  
 223 0.42 [95% CI 0.21-0.85]), compared to normal weight patients. Additionally, obese patients  
 224 had reduced odds of achieving cDAPSA-remission (OR<sub>adj</sub> 0.51 [95% CI 0.27-0.96]) and  
 225 DAS28-remission (OR<sub>adj</sub> 0.51 [95% CI 0.32-0.81]) within the first year. No differences were  
 226 observed across BMI categories on achievement of DAPSA-remLDA or treatment persistence  
 227 at the end of month-12.

228 The secondary analyses showed that extending the maximum follow-up to 15-months  
 229 resulted in similar findings to those from the 12-months analyses (**Table 2**). However, in the  
 230 9-months analyses, the associations of obesity with DAPSA-remission and with cDAPSA-  
 231 remission were no longer significant (**Table 2**).

232

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235

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

|  | n<br>sample<br>size | Maximum follow-up 9-months |                  |                  | Maximum follow-up 15-months |                  |                  |
|--|---------------------|----------------------------|------------------|------------------|-----------------------------|------------------|------------------|
|  |                     | n<br>vents                 | OR               | ORadj            | n<br>events                 | OR               | ORadj            |
| <b>MDA</b>   |                     |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>DAPSA-remission</b>                               |                     |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>DAPSA-remLDA</b>                                  |                     |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>cDAPSA-remission</b>                              |                     |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>DAS28-remission</b>                               |                     |                            |                  |                  |                             |                  |                  |
| 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) |
| <b>Treatment persistence at the end of follow-up</b> |                     |                            |                  |                  |                             |                  |                  |
| 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.

239  
 240 In the sensitivity analysis in which the respective composite disease activity score or  
 241 health standardized survey was included in the model, the previously observed findings in the  
 242 high BMI groups were attenuated, with the exception of obesity and achievement of MDA  
 243 (**Supplementary Table S2**). The sensitivity analysis excluding patients with missing  
 244 information on outcome during the one-year follow-up yielded stronger reduced odds of  
 245 achieving MDA and remission among abnormal BMI categories vs the normal weight group  
 246 (**Supplementary Table S3**). The sensitivity analysis excluding the 12 patients with BMI<18.5  
 247 yielded similar results to the main study findings (**Supplementary Table S4**).

1  
2 248 The frequency of achieved outcomes (with 12-months follow-up) per BMI category are  
3  
4 249 presented in **Figure 2**. Overall, 125 patients achieved MDA, 83 DAPSA-remission, 197  
5  
6 250 DAPSA-remLDA, 112 cDAPSA-remission, and 275 DAS28-remission within the first year.  
7  
8 251 Across all outcomes, patients with obesity had a lower prevalence of achieved outcomes.  
9  
10 252 DAS28-remission and treatment persistence had the highest prevalence in all groups, with  
11  
12 253 37.58% and 59.80% achieved among normal weight patients and 27.87% and 51.37% among  
13  
14 254 obese, respectively.  
15  
16

17  
18 255 The overlap of patients achieving the outcomes during the first year is illustrated in  
19  
20 256 **Figure 3**, complemented with numerical values in **Supplementary Table S5**. Among the 125  
21  
22 257 patients achieving MDA (66 normal weight, 40 overweight, 19 obese), 80 also achieved  
23  
24 258 DAPSA-remission, of which 48 (72.73%) were normal weight, 20 (50.00%) were overweight,  
25  
26 259 and 12 (63.16%) were obese. Similarly, among patient with MDA, 54 (81.82%) normal weight,  
27  
28 260 32 (80.00%) overweight, and 15 (78.95%) obese patients also achieved cDAPSA-remission.  
29  
30 261 Additionally, MDA overlapped with every remission outcome in 45 (68.18%) normal weight,  
31  
32 262 18 (45.00%) overweight, and 11 (57.89%) obese patients.  
33  
34  
35  
36

## 37 263 **DISCUSSION**

38  
39 264 This observational cohort study found that obese patients had a significant 49% to 58% reduced  
40  
41 265 odds of achieving MDA, DAPSA-remission, cDAPSA-remission, and DAS28-remission  
42  
43 266 within the first year, when compared to normal weight patients. Conversely, being overweight  
44  
45 267 was only associated with a reduced odds of achieving DAPSA remission. In both high BMI  
46  
47 268 categories, the association with achievement of DAPSA-remLDA within the first year and with  
48  
49 269 one-year treatment persistence, were not statistically significant. Among patients who achieved  
50  
51 270 MDA, the majority also achieved cDAPSA-remission.  
52  
53  
54

55  
56 271 Our findings on the association between obesity and lower probability of reaching MDA  
57  
58 272 and remission are consistent with other longitudinal observational studies.<sup>10,13,15</sup> In the  
59  
60 273 prospective study by Di Minno et al., obesity was associated with increased risk of not

1  
2 274 achieving MDA during a 12-months follow-up compared to patients with BMI<30 (hazard  
3  
4 275 ratio 4.90, 95%CI 3.04–7.87).<sup>13</sup> Eder et al. reported that, compared to normal weight patients  
5  
6 276 (BMI<25), overweight and obese patients had 34% and 47% significantly reduced odds of  
7  
8  
9 277 achieving MDA, respectively.<sup>10</sup> While we identified a similar OR in the overweight and obese  
10  
11 278 patients, our results in the overweight group were not statistically significant. In the study by  
12  
13 279 Højgaard et al., obesity was associated with 53% lower odds of achieving European Alliance  
14  
15 280 of Associations for Rheumatology (EULAR) good or moderate (EGOM) response.<sup>15</sup> While we  
16  
17 281 did not assess EGOM response, this is a DAS28-driven outcome, and the findings are in  
18  
19 282 agreement with our observed association between obesity and 49% reduced odds for DAS28-  
20  
21 283 remission. Conversely, Iannone et al. suggested no significant differences in DAS28-remission  
22  
23 284 rates across BMI categories.<sup>26</sup> However, they had a small sample size (135 patients), and their  
24  
25 285 observed lower remission rate in the obese vs normal weight patients was in line with our  
26  
27 286 findings.

28  
29  
30  
31  
32 287 Additionally, results from Højgaard et al. showed that compared to non-obese patients  
33  
34 288 (BMI<30), obese patients were associated with a 60% higher risk of TNFi discontinuation  
35  
36 289 during their study period (median follow-up of 1.5 years).<sup>15</sup> While our study did not yield an  
37  
38 290 association between BMI and treatment persistence, these contrasting findings may be  
39  
40 291 explained by the different methodologies. Højgaard et al. assessed the time to withdrawal using  
41  
42 292 a survival model, which gives high attention to early outcomes, while we investigated  
43  
44 293 persistence yes/no at a specific timepoint using logistic regression.

45  
46  
47  
48 294 In our study, MDA was the main outcome as it covers several aspects from the disease  
49  
50 295 presentation and consequences, and has been associated with patient's QoL and productivity.<sup>27</sup>  
51  
52 296 Additionally, McGagh and Coates suggested that the 66/68 joint counts provides a more  
53  
54 297 realistic picture of joint involvement in PsA, compared to the 28 joint counts, and highlighted  
55  
56 298 the benefits of including patient-reported outcomes.<sup>28</sup> Based on this, we identified DAPSA-  
57  
58 299 remission and cDAPSA-remission as optimal secondary outcomes. However, we expect that



1  
2 300 cDAPSA may be a better fit to study patients with abnormal BMI since obesity was associate  
3  
4 301 with elevated CRP in the general population.<sup>29–31</sup> This is further supported by the high overlap  
5  
6 302 of patients achieving MDA and cDAPSA-remission in our study, which was similar across  
7  
8  
9 303 every BMI group.

10  
11 304 Regarding the observed higher frequency of achievement of DAS28-remission compared  
12  
13 305 to other remission endpoints, this may be explained by its narrow focus on peripheral  
14  
15 306 manifestations, potentially underestimating residual disease activity. Nevertheless, the  
16  
17 307 consistency of the observed results on MDA and remission outcomes in the obese group  
18  
19 308 suggests that obesity affects peripheral joints, as well as disease-specific manifestations and  
20  
21 309 the patient's perspective. However, we note that the different outcome definitions led to  
22  
23 310 contrasting results in the overweight group, suggesting that the effect of overweight on the PsA  
24  
25 311 may not be fully captured by every remission definition. Similarly, the impact of obesity on  
26  
27 312 PsA clinical response was not consistent with the more clinically accessible outcome low  
28  
29 313 disease activity (DAPSA-remLDA).

30  
31  
32  
33  
34 314 The reasons for the lower response rates in obese patients could be multiple. High body  
35  
36 315 weight can affect the clearance and volume of distribution of b/tsDMARDs.<sup>32–34</sup> Adipose tissue  
37  
38 316 has a proinflammatory capacity,<sup>35</sup> which could negatively influence drug response. Finally, a  
39  
40 317 relationship between mechanical stress and triggering of musculoskeletal inflammation (deep  
41  
42 318 Köbner phenomenon) in psoriatic arthritis is discussed. Nevertheless, the observed lower odds  
43  
44 319 of achieving MDA or remission in the obese group is of interest, and the consistency across  
45  
46 320 the studied definitions of remission suggests that this effect may be reflected on several factors  
47  
48 321 of the PsA disease.

49  
50  
51  
52 322 Finally, as described elsewhere,<sup>12</sup> the prevalence of overweight and obesity were higher  
53  
54 323 among PsA patients in comparison to the general population in Switzerland (Switzerland 2017,  
55  
56 324 people >15 years old, 31% overweight and 11% obese).<sup>36</sup> Higher obesity prevalence among  
57  
58 325 PsA patients in comparison to the reference population was in agreement with prior studies.<sup>12</sup>  
59  
60



## 326 **Strengths and limitations**

327 In addition to the large sample size and availability of BMI information (often lacking in real-  
328 world-data), the key strength of this study is the use of several relevant clinical outcome  
329 definitions. While multiple approaches to assess PsA disease activity exist, no single one has  
330 been identified as sufficient<sup>37</sup> and the choice of the optimal measure remains challenging.<sup>28</sup> The  
331 consistency of the observed results on MDA and remission outcomes in the obese group  
332 reinforces the study findings. However, we did not look at unidimensional outcomes (e.g.,  
333 dactylitis) and this remains of interest for future studies. Additionally, while standard MDA  
334 definition includes Psoriasis Activity and Severity Index (PASI)  $\leq 1$  or body surface area (BSA)  
335  $\leq 3$ ,<sup>38</sup> due to data restrictions our MDA definition included a skin manifestation of “none” or  
336 “almost none”, as reported by the physician.

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

342 Intrinsic to real-world-data, missingness was a limitation. We addressed missingness at  
343 baseline with multiple imputation and missingness during follow-up with sensitivity analyses.  
344 Our results were mainly consistent among various sensitivity analyses. For example, in the  
345 secondary analysis excluding patients who missed information on the outcome during follow-  
346 up (instead of treating them as non-achievers of the respective outcome), supported the  
347 observed effect of obesity towards MDA and remission, which was even accentuated in this  
348 sensitivity analysis. Among secondary analyses varying the duration of follow-up, the 15-  
349 month analyses showed consistence with the main findings, and the reduced effect found in the  
350 9-months analyses may be explained by higher missingness of outcome information at shorter  
351 follow-up, and therefore lower number of observed events overall.

1  
2 352 Limitations to consider when interpreting the results include the potential  
3  
4 353 misclassification of patients in the BMI categories. While overweight and obesity are  
5  
6 354 commonly defined by BMI,<sup>39,40</sup> this lacks information on body composition. Thus, although  
7  
8  
9 355 data on waist circumference, skinfold thickness, and bioelectrical impedance may provide a  
10  
11 356 better patient classification, this information is extremely limited in real-world data.  
12  
13 357 Additionally, we classified patients with BMI<25 as normal weight, including patients with  
14  
15 358 BMI<18.5, who may be classified as underweight. This was done due to low prevalence of  
16  
17 359 underweight PsA patients in SCQM<sup>12</sup> and is consistent with previous practice in PsA<sup>10,26</sup> and  
18  
19 360 other inflammatory rheumatic diseases research in which the majority of studies combine  
20  
21 361 normal and underweight patients.<sup>41</sup>

22  
23  
24 362 It was suggested that obese patients may benefit from other non-TNFi b/tsDMARDs,  
25  
26 363 however, the evidence is limited.<sup>42</sup> Nevertheless, our results of a lower odds of achieving  
27  
28 364 remission may be largely driven by the high TNFi use in our cohort.

29  
30 365 Finally, since weight loss in overweight and obese patients was identified as a predictor  
31  
32 366 of MDA achievement,<sup>20</sup> it remains of interest to perform a similar study to this one but  
33  
34 367 stratifying the overweight and obese patients by those with and without weight loss.

## 38 39 40 368 **CONCLUSION**

41  
42 369 This study suggests that obesity in PsA patients is associated with at least a 50% reduction in  
43  
44 370 the likelihood of achieving MDA or remission within the first year after starting b/tsDMARD  
45  
46 371 therapy, when compared to normal weight patients. The consistency of findings across  
47  
48 372 definitions of remission suggests that obesity affects several factors of PsA disease.  
49  
50 373 Conversely, obesity was neither associated with the likelihood of achieving low disease activity  
51  
52 374 nor with treatment persistence. Finally, comparative analyses of b/tsDMARDs within BMI  
53  
54 375 groups is of interest and investigating the benefits of losing weight in this population remains  
55  
56 376 of interest.

## 377 **Author Contributions**

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

## 382 **Funding**

383 Not applicable. This research received no external funding.

## 384 **Conflict of interests**

385 None declared.

## 386 **Ethics approval**

387 This study was reviewed by the ethics commission of the Canton of Zurich (KEK: Req-2020-  
388 00045). Pseudonymized data, without access to the code key, was provided by the Swiss  
389 Clinical Quality Management in Rheumatic Diseases (SCQM) registry to the researchers.  
390 Therefore, the commission waived the need for a full ethics authorization.

## 391 **Patient consent for publication**

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

## 395 **Data Availability Statement**

396 Data belong to the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) and  
397 are available only with the approval and permission from the license holder (SCQM).

## 398 **Acknowledgments**

1  
2 399 We thank all patients and rheumatologists contributing to the SCQM registry, as well as the  
3  
4 400 entire SCQM staff. A list of rheumatology offices and hospitals which contribute to the SCQM  
5  
6 401 registry can be found at <http://www.scqm.ch/institutions>. A list of financial supporters of  
7  
8 402 SCQM can be found at <http://www.scqm.ch/sponsors>. We would like to add a personal thank  
9  
10  
11 403 you to Axel Finckh (University Hospitals of Geneva) for his input regarding the database. AMB  
12  
13 404 acknowledges that her professorship is partly endowed by the Swiss National Pharmacy  
14  
15 405 Association (PharmaSuisse) and the ETH Foundation.

## 18 406 **Supplementary Material**

20  
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## 42 416 **REFERENCES**

43  
44  
45 417 1 Kumthekar A, Ogdie A. Obesity and Psoriatic Arthritis: A Narrative Review. *Rheumatol*  
46 418 *Ther* 2020; **7**: 447–56.

47  
48 419 2 Salaffi F, De Angelis R, Grassi W, MArche Pain Prevalence, INvestigation Group  
49 420 (MAPPING) study. Prevalence of musculoskeletal conditions in an Italian population  
50 421 sample: results of a regional community-based study. I. The MAPPING study. *Clin Exp*  
51 422 *Rheumatol* 2005; **23**: 819–28.

52  
53  
54 423 3 Ogdie A, Weiss P. The Epidemiology Psoriatic Arthritis. *Rheum Dis Clin North Am* 2015;  
55 424 **41**: 545–68.

56  
57 425 4 Scotti L, Franchi M, Marchesoni A, Corrao G. Prevalence and incidence of psoriatic  
58 426 arthritis: A systematic review and meta-analysis. *Semin Arthritis Rheum* 2018; **48**: 28–34.

- 1  
2 427 5 Porta S, Otero-Losada M, Kölliker Frers RA, Cosentino V, Kerzberg E, Capani F.  
3 428 Adipokines, Cardiovascular Risk, and Therapeutic Management in Obesity and Psoriatic  
4 429 Arthritis. *Front Immunol* 2021; **11**. DOI:10.3389/fimmu.2020.590749.
- 6 430 6 Gossec L, Smolen JS, Ramiro S, *et al*. European League Against Rheumatism (EULAR)  
7 431 recommendations for the management of psoriatic arthritis with pharmacological therapies:  
8 432 2015 update. *Annals of the Rheumatic Diseases* 2016; **75**: 499–510.
- 11 433 7 Gossec L, Baraliakos X, Kerschbaumer A, *et al*. EULAR recommendations for the  
12 434 management of psoriatic arthritis with pharmacological therapies: 2019 update. *Annals of*  
13 435 *the Rheumatic Diseases* 2020; **79**: 700–12.
- 15 436 8 Gupta S, Syrimi Z, Hughes DM, Zhao SS. Comorbidities in psoriatic arthritis: a systematic  
16 437 review and meta-analysis. *Rheumatol Int* 2021; **41**: 275–84.
- 19 438 9 Bhole VM, Choi HK, Burns LC, *et al*. Differences in body mass index among individuals  
20 439 with PsA, psoriasis, RA and the general population. *Rheumatology* 2012; **51**: 552–6.
- 22 440 10 Eder L, Thavaneswaran A, Chandran V, Cook RJ, Gladman DD. Obesity is associated with  
23 441 a lower probability of achieving sustained minimal disease activity state among patients with  
24 442 psoriatic arthritis. *Ann Rheum Dis* 2015; **74**: 813–7.
- 26 443 11 Eder L, Abji F, Rosen CF, Chandran V, Gladman DD. The Association Between Obesity  
27 444 and Clinical Features of Psoriatic Arthritis: A Case-control Study. *J Rheumatol* 2017; **44**:  
28 445 437–43.
- 31 446 12 Vallejo-Yagüe E, Burkard T, Möller B, Finckh A, Burden AM. Comparison of Psoriatic  
32 447 Arthritis and Rheumatoid Arthritis Patients across Body Mass Index Categories in  
33 448 Switzerland. *Journal of Clinical Medicine* 2021; **10**: 3194.
- 35 449 13 di Minno MND, Peluso R, Iervolino S, *et al*. Obesity and the prediction of minimal disease  
36 450 activity: a prospective study in psoriatic arthritis. *Arthritis Care Res (Hoboken)* 2013; **65**:  
37 451 141–7.
- 39 452 14 Lupoli R, Pizzicato P, Scalera A, *et al*. Impact of body weight on the achievement of minimal  
40 453 disease activity in patients with rheumatic diseases: a systematic review and meta-analysis.  
41 454 *Arthritis Res Ther* 2016; **18**: 297.
- 44 455 15 Højgaard P, Glinborg B, Kristensen LE, Gudbjornsson B, Love TJ, Dreyer L. The influence  
45 456 of obesity on response to tumour necrosis factor- $\alpha$  inhibitors in psoriatic arthritis: results  
46 457 from the DANBIO and ICEBIO registries. *Rheumatology* 2016; **55**: 2191–9.
- 48 458 16 Singh S, Facciorusso A, Singh AG, *et al*. Obesity and response to anti-tumor necrosis factor- $\alpha$   
49 459 agents in patients with select immune-mediated inflammatory diseases: A systematic  
50 460 review and meta-analysis. *PLoS One* 2018; **13**: e0195123.
- 53 461 17 Versini M, Jeandel P-Y, Rosenthal E, Shoenfeld Y. Obesity in autoimmune diseases: Not a  
54 462 passive bystander. *Autoimmunity Reviews* 2014; **13**: 981–1000.
- 56 463 18 Russolillo A, Iervolino S, Peluso R, *et al*. Obesity and psoriatic arthritis: from pathogenesis  
57 464 to clinical outcome and management. *Rheumatology* 2013; **52**: 62–7.
- 59 465 19 Neumann E, Hasseli R, Ohl S, Lange U, Frommer KW, Müller-Ladner U. Adipokines and  
60 466 Autoimmunity in Inflammatory Arthritis. *Cells* 2021; **10**. DOI:10.3390/cells10020216.

- 1  
2 467 20 Minno MNDD, Peluso R, Iervolino S, *et al.* Weight loss and achievement of minimal disease  
3 468 activity in patients with psoriatic arthritis starting treatment with tumour necrosis factor  $\alpha$   
4 469 blockers. *Annals of the Rheumatic Diseases* 2014; **73**: 1157–62.
- 5  
6 470 21 Costa L, Caso F, Ramonda R, *et al.* Metabolic syndrome and its relationship with the  
7 471 achievement of minimal disease activity state in psoriatic arthritis patients: an observational  
8 472 study. *Immunol Res* 2015; **61**: 147–53.
- 9  
10 473 22 Die SCQM Foundation (Swiss Clinical Quality Management in Rheumatic Diseases).  
11 474 <https://www.scqm.ch/en/ueber-uns/> (accessed May 18, 2021).
- 12  
13  
14 475 23 Coates LC, Strand V, Wilson H, *et al.* Measurement properties of the minimal disease  
15 476 activity criteria for psoriatic arthritis. *RMD Open* 2019; **5**. DOI:10.1136/rmdopen-2019-  
16 477 001002.
- 17  
18 478 24 Buuren S van, Groothuis-Oudshoorn K. mice: Multivariate Imputation by Chained  
19 479 Equations in R. *Journal of Statistical Software* 2011; **45**: 1–67.
- 20  
21 480 25 R Core Team (2020). R: A language and environmental for statistical computing. R  
22 481 Foundation for Statistical Computing, Vienna, Austria. <https://www.r-project.org/>  
23 482 (accessed May 14, 2021).
- 24  
25  
26 483 26 Iannone F, Fanizzi R, Scioscia C, Anelli MG, Lapadula G. Body mass does not affect the  
27 484 remission of psoriatic arthritis patients on anti-TNF- $\alpha$  therapy. *Scandinavian Journal of*  
28 485 *Rheumatology* 2013; **42**: 41–4.
- 29  
30 486 27 Coates LC, Orbai A-M, Morita A, *et al.* Achieving minimal disease activity in psoriatic  
31 487 arthritis predicts meaningful improvements in patients' health-related quality of life and  
32 488 productivity. *BMC Rheumatology* 2018; **2**: 24.
- 33  
34  
35 489 28 McGagh D, Coates LC. Assessment of the many faces of PsA: single and composite  
36 490 measures in PsA clinical trials. *Rheumatology* 2020; **59**: i29–36.
- 37  
38 491 29 Yudkin JS, Stehouwer CDA, Emeis JJ, Coppack SW. C-Reactive Protein in Healthy  
39 492 Subjects: Associations With Obesity, Insulin Resistance, and Endothelial Dysfunction.  
40 493 *Arteriosclerosis, Thrombosis, and Vascular Biology* 1999; **19**: 972–8.
- 41  
42  
43 494 30 Hak AE, Stehouwer CDA, Bots ML, *et al.* Associations of C-Reactive Protein With  
44 495 Measures of Obesity, Insulin Resistance, and Subclinical Atherosclerosis in Healthy,  
45 496 Middle-Aged Women. *Arteriosclerosis, Thrombosis, and Vascular Biology* 1999; **19**: 1986–  
46 497 91.
- 47  
48 498 31 Visser M. Elevated C-Reactive Protein Levels in Overweight and Obese Adults. *JAMA*  
49 499 1999; **282**: 2131.
- 50  
51  
52 500 32 Sharma S, Eckert D, Hyams JS, *et al.* Pharmacokinetics and exposure-efficacy relationship  
53 501 of adalimumab in pediatric patients with moderate to severe Crohn's disease: results from a  
54 502 randomized, multicenter, phase-3 study. *Inflamm Bowel Dis* 2015; **21**: 783–92.
- 55  
56 503 33 Fasanmade AA, Adedokun OJ, Ford J, *et al.* Population pharmacokinetic analysis of  
57 504 infliximab in patients with ulcerative colitis. *Eur J Clin Pharmacol* 2009; **65**: 1211–28.
- 58  
59 505 34 Ternant D, Aubourg A, Magdelaine-Beuzelin C, *et al.* Infliximab pharmacokinetics in  
60 506 inflammatory bowel disease patients. *Ther Drug Monit* 2008; **30**: 523–9.



- 1  
2 507 35Versini M, Jeandel P-Y, Rosenthal E, Shoenfeld Y. Obesity in autoimmune diseases: not a  
3 508 passive bystander. *Autoimmun Rev* 2014; **13**: 981–1000.  
4
- 5 509 36Statistik B für. Übergewicht und Adipositas - Schweizerische Gesundheitsbefragung 2017 |  
6 510 Publikation. Bundesamt für Statistik. 2020; published online Sept 3.  
7 511 <https://www.bfs.admin.ch/asset/de/14147705> (accessed June 5, 2022).  
8
- 9  
10 512 37Gulfe A, Geborek P, Saxne T. Response criteria for rheumatoid arthritis in clinical practice:  
11 513 how useful are they? *Ann Rheum Dis* 2005; **64**: 1186–9.  
12
- 13 514 38Coates LC, Franssen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis:  
14 515 a proposed objective target for treatment. *Ann Rheum Dis* 2010; **69**: 48–53.  
15
- 16 516 39Body mass index - BMI. [https://www.euro.who.int/en/health-topics/disease-](https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi)  
17 517 [prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi](https://www.euro.who.int/en/health-topics/disease-prevention/nutrition/a-healthy-lifestyle/body-mass-index-bmi) (accessed June 23, 2021).  
18
- 19 518 40Obesity and overweight. [https://www.who.int/news-room/fact-sheets/detail/obesity-and-](https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight)  
20 519 [overweight](https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight) (accessed July 8, 2021).  
21
- 22  
23 520 41Lee Y, Kwan Y, Lim K, *et al.* A systematic review of the association of obesity with the  
24 521 outcomes of inflammatory rheumatic diseases. *smelj* 2019; **60**: 270–80.  
25
- 26 522 42Queiro R. Cardiometabolic comorbidity in the selection of treatment in spondyloarthritis:  
27 523 one step closer to truly personalized medicine? *Expert Opin Biol Ther* 2021; **21**: 1539–41.  
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2 528 **FIGURE LEGENDS**  
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7 530 (Attached as JPG)

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9 531 **Figure 1.** Results from the multivariable logistic regression investigating the association  
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11 532 between body mass index (BMI) categories and various clinical outcomes. Maximum follow-  
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13 533 up 12-months.  
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23 537 **Figure 2.** Distribution of patients achieving the study primary and secondary outcomes within  
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25 538 the first year, and percentage of patients achieving treatment persistence at the end of month-  
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27 539 12, stratified by body mass index (BMI) category. Abbreviations: MDA Minimal Disease  
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29 540 Activity; DAPSRem Disease Activity for Psoriatic Arthritis (DAPSA) remission;  
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31 541 DAPSRemLDA DAPSA remission or low disease activity; cDAPSRem clinical DAPSA  
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33 542 remission; DAS28rem 28-joint disease activity score remission.  
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43 546 **Figure 3.** Venn Diagram depicting the number of patients (counts) achieving the study  
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45 547 individual primary and secondary outcomes within the first year, overall and stratifying by  
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47 548 body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSRem  
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49 549 Disease Activity for Psoriatic Arthritis (DAPSA) remission; DAPSRemLDA DAPSA  
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51 550 remission or low disease activity; cDAPSRem clinical DAPSA remission; DAS28rem 28-  
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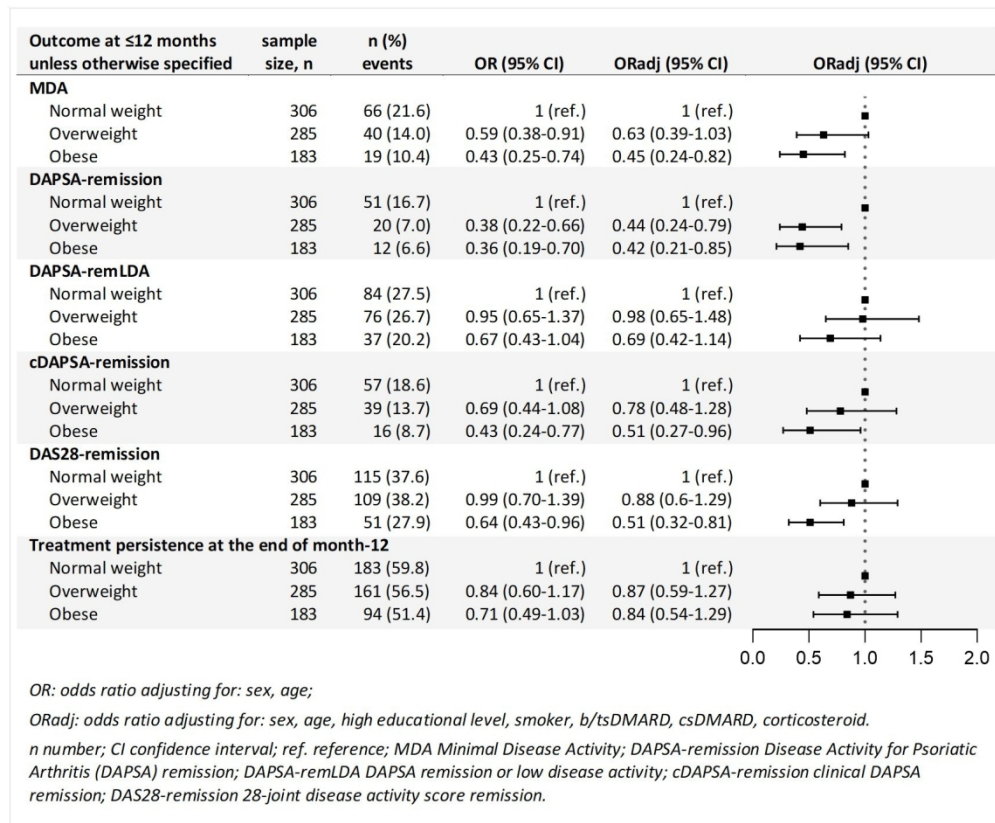


Figure 1. Results from the multivariable logistic regression investigating the association between body mass index (BMI) categories and various clinical outcomes. Maximum follow-up 12-months.

301x249mm (144 x 144 DPI)

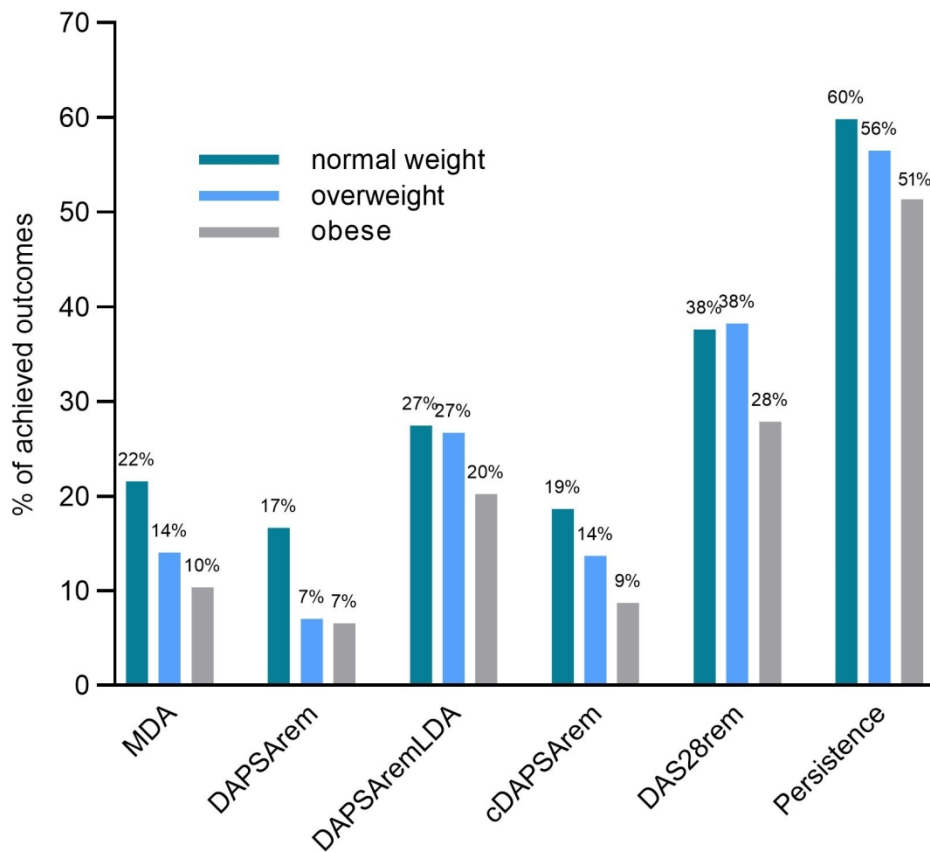


Figure 2. Distribution of patients achieving the study primary and secondary outcomes within the first year, and percentage of patients achieving treatment persistence at the end of month-12, stratified by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSAreM Disease Activity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

306x275mm (144 x 144 DPI)

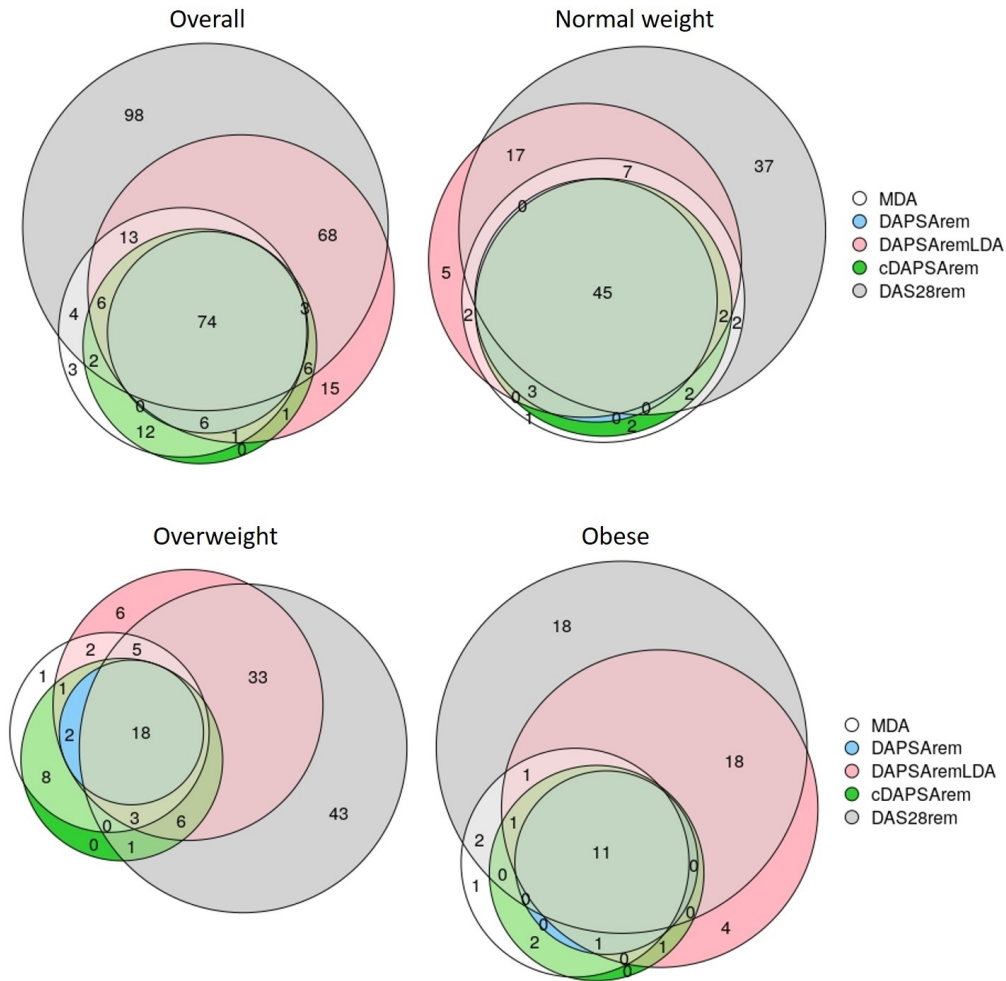


Figure 3. Venn Diagram depicting the number of patients (counts) achieving the study individual primary and secondary outcomes within the first year, overall and stratifying by body mass index (BMI) category. Abbreviations: MDA Minimal Disease Activity; DAPSArem Disease Activity for Psoriatic Arthritis (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

# 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

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

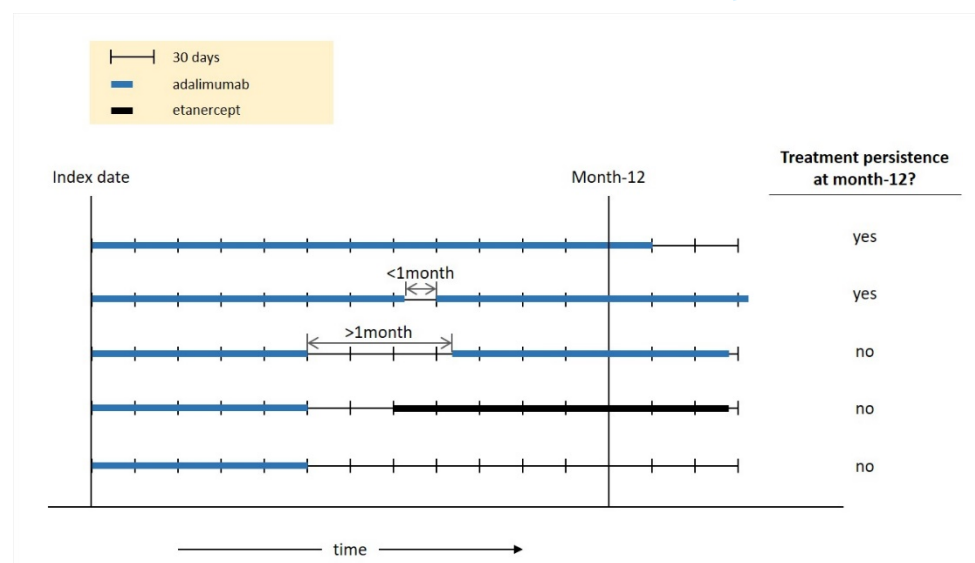
$$(2) \text{ DAPSA} = \text{sjc66} + \text{tjc68} + \text{PatActivity} + \text{PatPain} + \text{CRP}$$

$$(3) \text{ cDAPSA} = \text{sjc66} + \text{tjc68} + \text{PatActivity} + \text{PatPain}$$

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

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

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



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

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4 **Supplementary Text S1.** Additional information on covariates.  
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6 High education was defined as '*höhere Fachschule*' (university of applied sciences), or  
7 '*Universitätsstudium*' (university study); and the no category for this variable was defined by  
8 '*obligatorische Schule*' (compulsory school), '*Berufslehre*' (apprenticeship), or '*Maturitätsschule*' (3-4  
9 year high school that enables direct admission to Universities school)'.  
10

11 Smoker (ever smoker) was defined by at least one record of smoker prior index date.  
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14 Patient and physician assessments on disease activity, pain, or skin manifestations, as well as  
15 medication, disease specific manifestations (musculoskeletal manifestations, dactylitis, enthesitis,  
16 sacrolitis, spinal involvement, coxitis, peripheral arthritis, nail manifestations) and comorbidities are  
17 recorded as specific variables in SCQM.  
18

19 Information on comorbidities was extracted from the SCQM health issues dataset or table, which  
20 contains patient reported information. Lack of disease or health issue was assumed unless otherwise  
21 stated. Cardiovascular event/disease included cerebrovascular disease, coronary heart disease, deep  
22 vein thrombosis, heart infarct, heart insufficiency, peripheral vascular disease, pulmonary embolism,  
23 hypertension, hypotension, other cardiovascular disease, and other heart disease, ever before the  
24 index date. Diabetes included type I and type II, ever before index date. Other metabolic problems  
25 included adrenal disease, thyroid disease, diseases of other endocrine glands, dysfunctions of water  
26 electrolyte balance or acid alkaline balance, hyperlipidaemia, and hyperuricemia, within the 6-months  
27 prior index date. Depression/anxiety includes depression and anxiety, within the 6-months prior index  
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**Supplementary Table S1.** Variables included in the multiple imputation.

| Variable  | Version 1 Included | Version 2 Included | Predicted | Predictor        | Method                          | Missingness | Levels   | Range         |
|---|--------------------|--------------------|-----------|------------------|---------------------------------|-------------|--|---------------|
| Outcome <sup>a</sup> (MDA/DAPSArem/DAPSAremLDA/Persistence) | yes                | -                  | -         | yes              | -                               | -           | yes; no.   | -             |
| Outcome <sup>a</sup> (DAS28rem)                             | -                  | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Patient ID  | yes                | yes                | -         | -                | -                               | -           | -  | 1-774         |
| BMI category  | yes                | yes                | -         | -                | -                               | -           | normal weight; overweight; obese.  | -             |
| BMI kg/m <sup>2</sup>                                       | 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 <sup>b</sup> | passive imputation <sup>d</sup> | 298 (38.5)  | -  | 0.10 - 121    |
| DAS28   | -                  | yes                | yes       | yes <sup>c</sup> | passive imputation <sup>e</sup> | 99 (12.79)  | -  | 0.20 - 7.60   |
| HAQ (0-3)   | yes                | yes                | yes       | yes              | pmm                             | 167 (21.58) | -  | 0 - 3         |
| SF-12mcs (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.   | -             |
| Sacroiliitis  | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Enthesitis  | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Spinal involvement  | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Coxitis   | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |
| Dactylitis  | yes                | yes                | -         | yes              | -                               | -           | yes; no.   | -             |

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

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

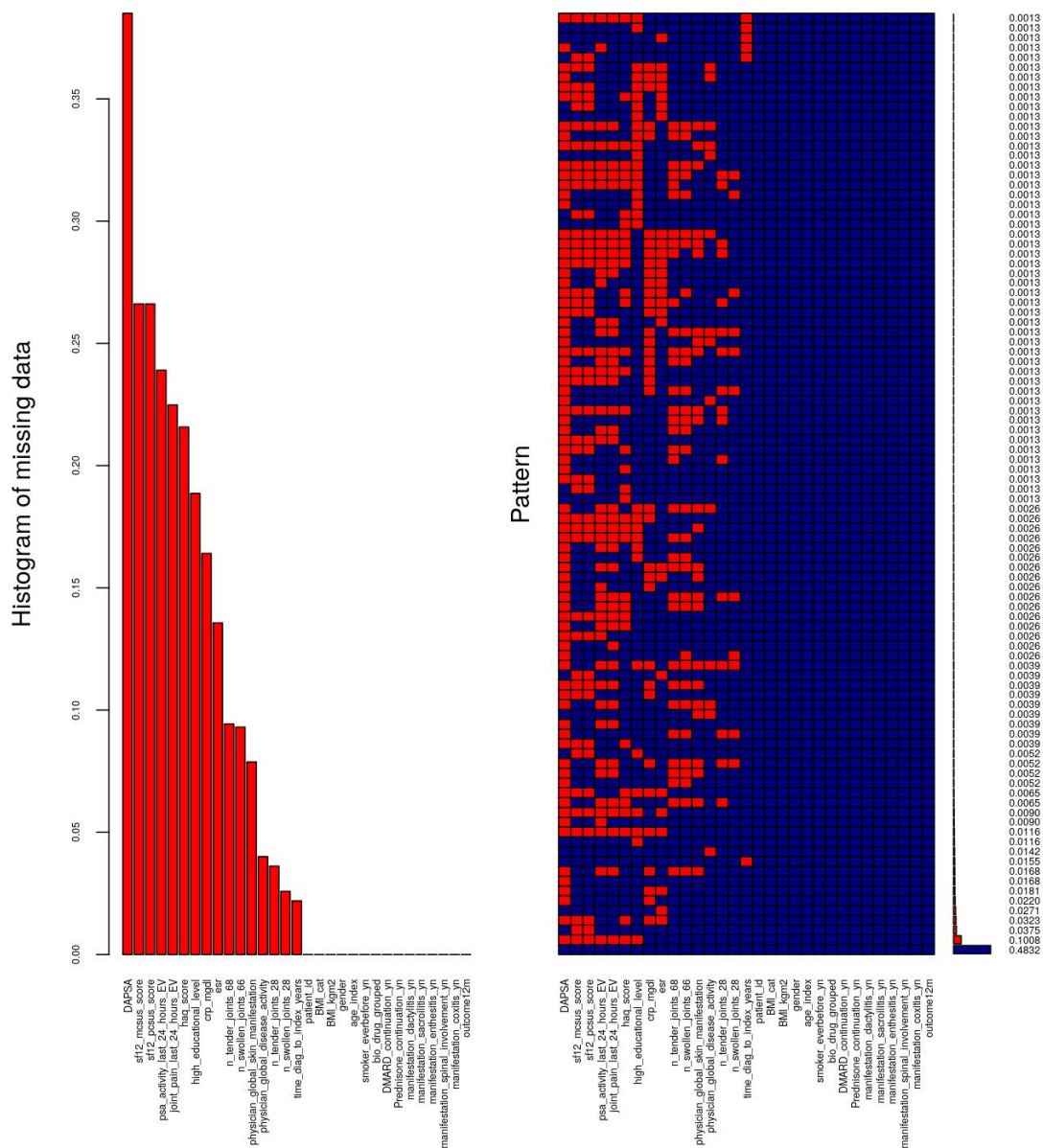
<sup>b</sup> DAPSA not used as predictor for: sjc66, tjc68, PatActivity, PatPain, CRP.

<sup>c</sup> DAS28 not used as predictor for: sjc28, tjc28, ESR.

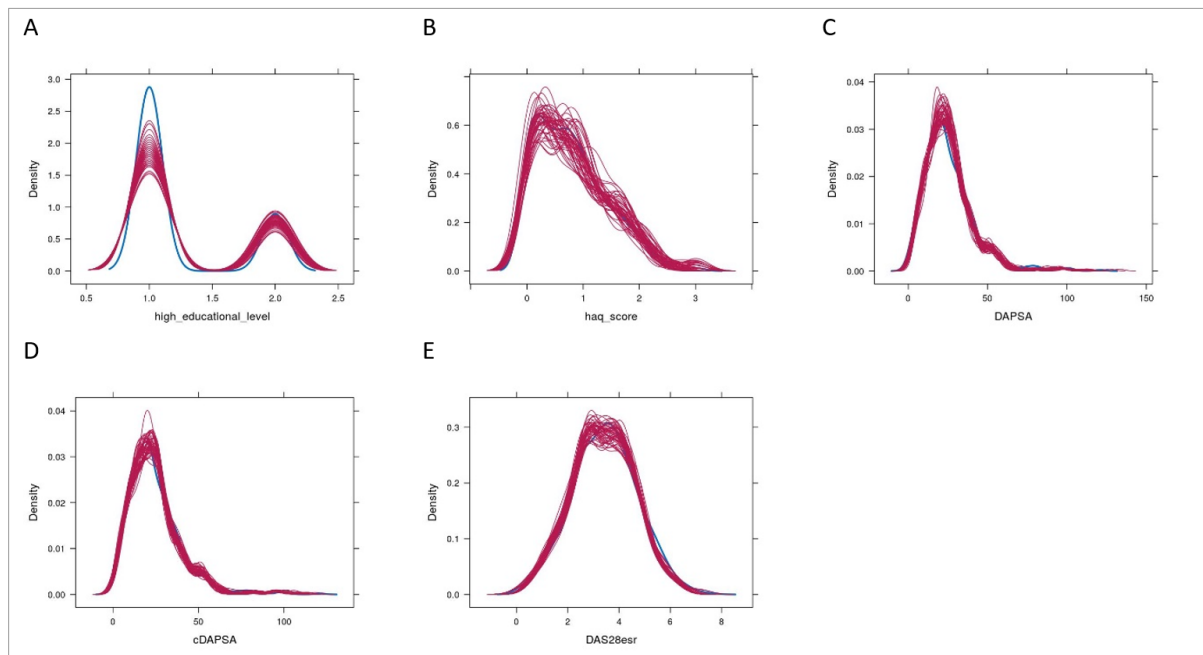
<sup>d</sup> DAPSA passive imputation:  $DAPSA = sjc66 + tjc68 + PatActivity + PatPain + CRP$

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

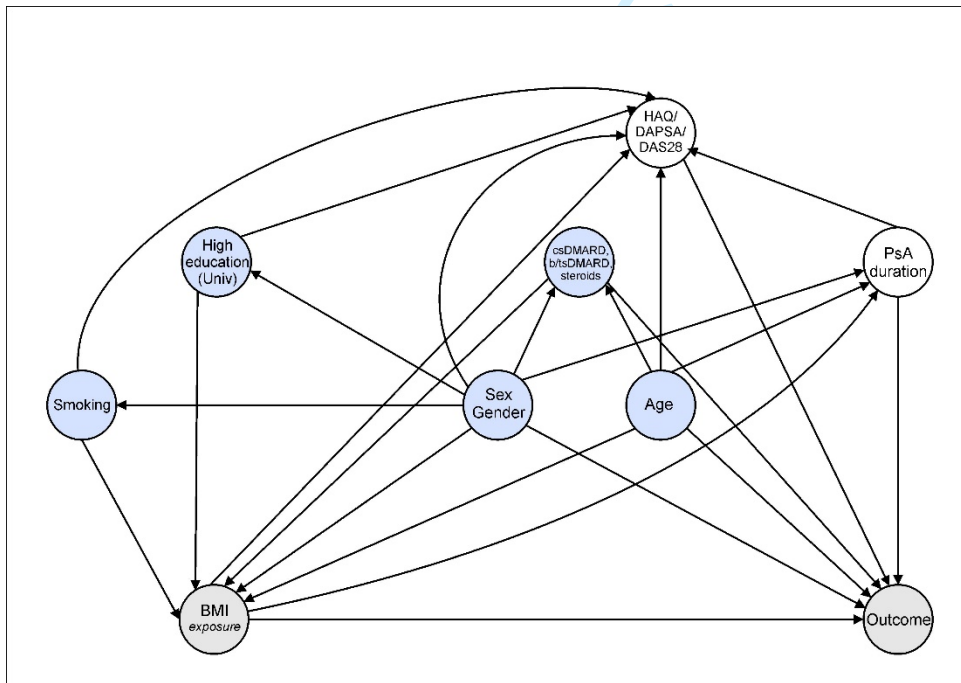




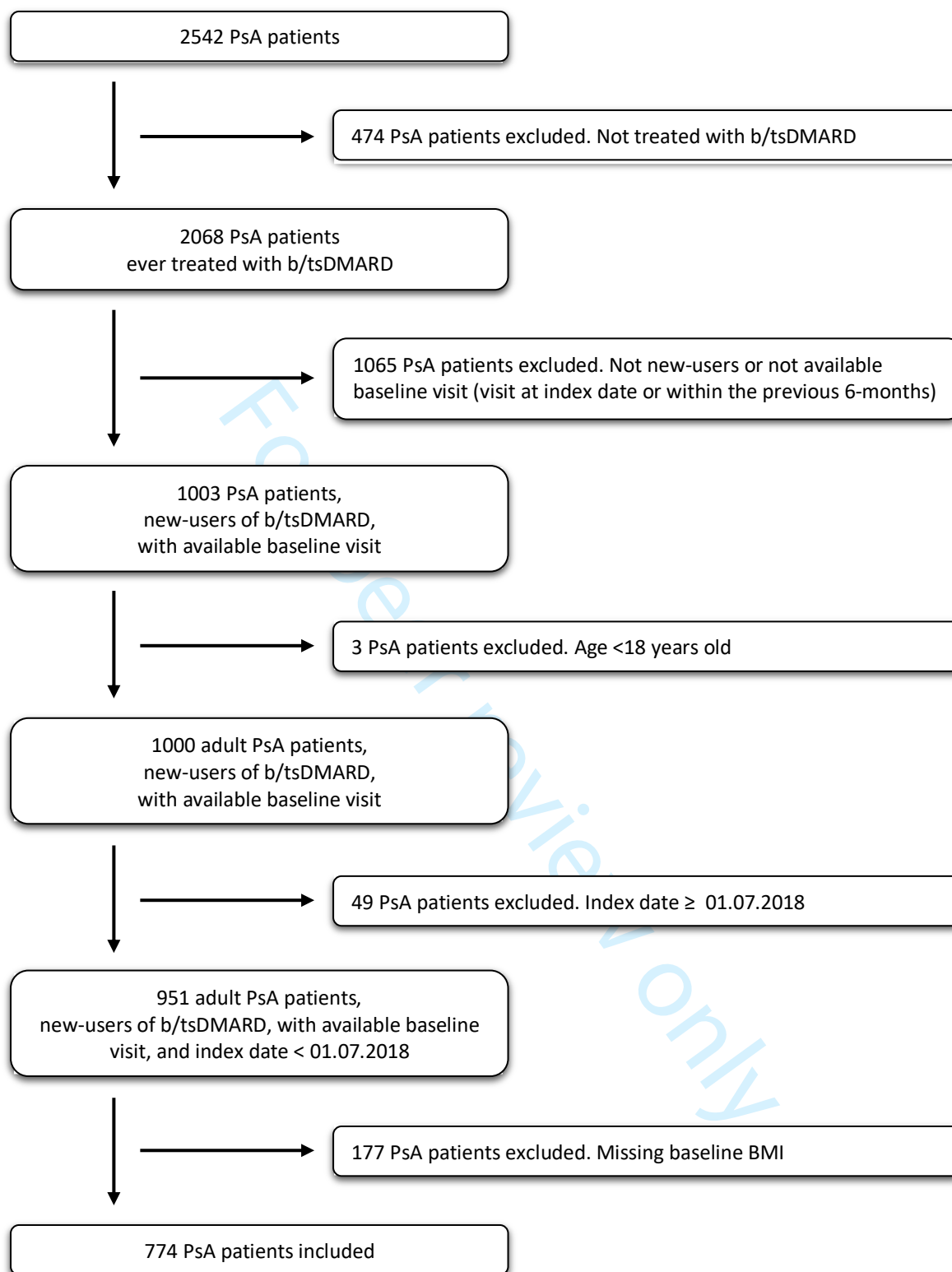
**Supplementary Figure S2.** Graphical representation of the missingness among baseline variables included in the imputations for primary analysis (i.e., achievement of Minimal Disease Activity (MDA) within the first year after index date). The 48.32% of patients had complete information on all the included 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 rationale 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 <sup>c</sup> (95% CI) | n events                    | ORadj <sup>c</sup> (95% CI) | n events                    | ORadj <sup>c</sup> (95% CI) |
| <b>MDA</b>                   |               |                            |                             |                             |                             |                             |                             |
| 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)             |
| <b>DAPSA-remission</b>       |               |                            |                             |                             |                             |                             |                             |
| 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)               |
| <b>DAPSA-remLDA</b>          |               |                            |                             |                             |                             |                             |                             |
| 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)            |
| <b>cDAPSA-remission</b>      |               |                            |                             |                             |                             |                             |                             |
| 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)             |
| <b>DAS28-remission</b>       |               |                            |                             |                             |                             |                             |                             |
| 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)            |
| <b>Treatment persistence</b> |               |                            |                             |                             |                             |                             |                             |
| Normal weight                | 306           | 204 (66.7)                 | 1 (ref.)                    | 183 (59.8)                  | 1 (ref.)                    | 159 (52.0)                  | 1 (ref.)                    |
| Overweight                   | 285           | 184 (64.6)                 | 0.92 (0.61-1.4)             | 161 (56.5)                  | 0.88 (0.59-1.3)             | 148 (51.9)                  | 1.04 (0.71-1.54)            |
| Obese                        | 183           | 111 (60.7)                 | 0.92 (0.56-1.49)            | 94 (51.4)                   | 0.92 (0.58-1.46)            | 81 (44.3)                   | 1.04 (0.66-1.64)            |

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

Abbreviations: n number; CI confidence interval; ref. reference; 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 <sup>a</sup> (95% CI) | ORadj <sup>b</sup> (95% CI) | ORadj <sup>c</sup> (95% CI) |
| <b>MDA</b>              |   |            |                          |                             |                             |
| 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)            |
| <b>DAPSA-remission</b>  |   |            |                          |                             |                             |
| 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)            |
| <b>DAPSA-remLDA</b>     |   |            |                          |                             |                             |
| 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)            |
| <b>cDAPSA-remission</b> |   |            |                          |                             |                             |
| 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)            |
| <b>DAS28-remission</b>  |   |            |                          |                             |                             |
| Normal weight           | 159   | 115 (72.3) | 1 (ref.)                 | 1 (ref.)                    | 1 (ref.)                    |
| Overweight              | 153   | 109 (71.2) | 0.86 (0.51-1.46)         | 0.55 (0.3-1.01)             | 0.57 (0.28-1.14)            |
| Obese                   | 89  | 51 (57.3)  | 0.48 (0.27-0.86)         | 0.3 (0.15-0.6)              | 0.37 (0.17-0.81)            |

OR: odds ratio adjusting for: sex, age;

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

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

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

**Supplementary Table S4.** Sensitivity analyses, excluding the 12 patients with body mass index (BMI) <18.5 kg/m<sup>2</sup>. 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<br>(Excluding BMI<18.5)         | n<br>sample size | Maximum follow-up 12-months |                  |                  |
|--|------------------|-----------------------------|------------------|------------------|
|  |                  | n<br>vents                  | OR               | ORadj            |
| <b>MDA</b>   |                  |                             |                  |                  |
| 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) |
| <b>DAPSA-remission</b>                               |                  |                             |                  |                  |
| 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) |
| <b>DAPSA-remLDA</b>                                  |                  |                             |                  |                  |
| 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) |
| <b>cDAPSA-remission</b>                              |                  |                             |                  |                  |
| 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) |
| <b>DAS28-remission</b>                               |                  |                             |                  |                  |
| 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) |
| <b>Treatment persistence at the end of follow-up</b> |                  |                             |                  |                  |
| 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 |          |             |           |          | Overall<br>(n=774)<br>(counts) | Normal weight<br>(n=306)<br>(counts) | Overweight<br>(n=285)<br>(counts) | Obese<br>(n=183)<br>(counts) |
|-------------------|----------|-------------|-----------|----------|--------------------------------|--------------------------------------|-----------------------------------|------------------------------|
| MDA               | DAPSArem | DAPSAremLDA | cDAPSArem | DAS28rem |                                |                                      |                                   |                              |
| ✓                 | -        | -           | -         | -        | 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**Enriqueta Vallejo-Yagüe<sup>1</sup>, Theresa Burkard<sup>1</sup>, Andrea M. Burden<sup>1</sup><sup>1</sup> Department of Chemistry and Applied Biosciences, Institute of Pharmaceutical Sciences, ETH Zurich, Zurich, Switzerland.STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

|                              | Item No | Recommendation   | Page No                               |
|------------------------------|---------|--|---------------------------------------|
| <b>Title and abstract</b>    | 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                                     |
| <b>Introduction</b>          |         |  |                                       |
| 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                                     |
| <b>Methods</b>               |         |  |                                       |
| 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/<br>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;<br>Supplementary<br>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                                   |



|                          |     |   |   |
|--------------------------|-----|---|---|
| <b>Results</b>           |     |   |   |
| 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<br>(b) Give reasons for non-participation at each stage<br>(c) Consider use of a flow diagram   | Supplementary Figure S5<br><br>Supplementary Figure S5<br>Supplementary Figure S5 |
| Descriptive data         | 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders<br>(b) Indicate number of participants with missing data for each variable of interest<br>(c) Summarise follow-up time (eg, average and total amount)  | 9<br><br>Table 1<br><br>NA (see page 7)   |
| Outcome data             | 15* | Report numbers of outcome events or summary measures over time  | Figure 1;<br>Table 2;<br>Figure 2;<br>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<br>(b) Report category boundaries when continuous variables were categorized<br>(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period | 11-12;<br>Figure 1;<br>Table 2<br><br>6-7 (exposure and outcome)<br>-             |
| Other analyses           | 17  | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses  | 12-13   |
| <b>Discussion</b>        |     |   |   |
| 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   | -   |
| <b>Other information</b> |     |   |   |
| 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>.