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Ying Ying Leung, Lihi Eder, Ana-Maria Orbai, Laura C Coates, Maarten de Wit, et al.. Association between obesity and likelihood of remission or low disease activity status in psoriatic arthritis applying index-based and patient-based definitions of remission: a cross-sectional study. RMD Open, 2023, 9 (3), pp.e003157. 10.1136/rmdopen-2023-003157. hal-04306101

HAL Id: hal-04306101 https://hal.sorbonne-universite.fr/hal-04306101

Submitted on 24 Nov 2023

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ORIGINAL RESEARCH

Association between obesity and likelihood of remission or low disease activity status in psoriatic arthritis applying index-based and patient-based definitions of remission: a cross-sectional study

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To cite: Leung YY. Eder L. Orbai A-M, et al. Association between obesity and likelihood of remission or low disease activity status in psoriatic arthritis applying index-based and patient-based definitions of remission: a cross-sectional study. RMD Open 2023:9:e003157. doi:10.1136/ rmdopen-2023-003157

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10. 1136/rmdopen-2023-003157).

Received 14 March 2023 Accepted 29 May 2023



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ABSTRACT

Objectives We aimed to evaluate whether obese patients with psoriatic arthritis (PsA) were less likely to be in remission/low disease activity (LDA).

Methods We used data from the ReFlaP, an international multi-centre cohort study (NCT03119805), which recruited consecutive adults with definite PsA (disease duration ≥ 2 years) from 14 countries. Demographics, clinical data, comorbidities, and patient-reported outcomes were collected. Remission/LDA was defined as Very Low Disease Activity (VLDA)/minimal disease activity (MDA), Disease Activity in PSoriatic Arthritis (DAPSA) ≤4/≤14, or by patients' opinion. Obesity was defined as physician-reported and/or body mass index ≥30 kg/m². We evaluated the association between obesity and the presence of remission/LDA, with adjustment in multivariable regression models.

Results Among 431 patients (49.3% women), 136 (31.6%) were obese. Obese versus non-obese patients were older, more frequently women, had higher tender joint and enthesitis counts and worse pain, physical function and health-related quality of life. Obese patients were less likely to be in VLDA; DAPSA remission and MDA, with adjusted ORs of 0.31 (95% Cl 0.13 to 0.77); 0.39 (95% CI 0.19 to 0.80) and 0.61 (95% CI 0.38 to 0.99), respectively. Rates of DAPSA-LDA and patient-reported remission/LDA were similar for obese and non-obese patients. Conclusion PsA patients with comorbid obesity were 2.5-3 folds less likely to be in remission/LDA by composite scores compared with non-obese patients; however, remission/LDA rates were similar based on the patients' opinion. PsA patients with comorbid obesity may have different disease profiles and require individualised management.

INTRODUCTION

Psoriatic arthritis (PsA) is a systemic immune-related rheumatic disease with many clinical manifestations. In addition

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ A few Caucasian studies have indicated that patients with obesity may be less likely to achieve remission.

WHAT THIS STUDY ADDS

- ⇒ Congruent with the existing literature, we have shown from an international multicentre study that obesity is associated with higher pain scores and worse physical function and health-related quality of life. Patients with comorbid obesity also had lower probability of the presence of remission/low disease activity (LDA) by composite scores.
- ⇒ The differences in rates of remission/LDA between obese and non-obese patients according to patients' opinion were lower.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ This highlights the importance of recognising and managing obesity as an important comorbidity to improve the care of patients with psoriatic arthritis.

to musculoskeletal and skin disease, the key domains relevant to both physicians and patients include physical function, fatigue, patient global assessment (PGA) and healthrelated quality of life (HR-QoL).^{2 3} PsA is also associated with an increased prevalence of metabolic and cardiovascular comorbidities, such as obesity, hypertension, hyperlipidaemia, type II diabetes and coronary heart disease. According to the treat-to-target management strategy (T2T), achieving remission (or alternatively, low disease activity, LDA) is an important target.^{4 5} Achieving a

state of remission or LDA is associated with improved patient-reported outcomes (PROs) and physical function and less radiographic progression.⁶ It may also be associated with lower atherosclerosis burden in the long term.⁷

Some indices have been developed to assess or define states of remission or LDA, including the binary states of Very Low Disease Activity (VLDA) and minimal disease activity (MDA) and the continuous score Disease Activity in PSoriatic Arthritis (DAPSA) with cut-offs for remission and LDA. ⁸⁹ To date, there is no consensus on which remission target is best to guide treatment in clinical practice. ⁴ In addition, these indices may not necessarily reflect the patients' opinion on their status. ^{10 11} We previously reported that the agreement between remission/LDA by composite indices and patients' opinion was only moderate to good. ¹⁰

Obesity is common among patients with PsA and is an important comorbidity. Desity is more prevalent among patients with PsA than in patients with rheumatoid arthritis or the general population. Obesity is a risk factor for the development of psoriasis in the general population, Hall it is also associated with an increased risk of PsA among those with psoriasis. Obesity may be a consequence of a sedentary lifestyle due to musculoskeletal inflammation and pain or psychological distress from skin disease. Adipokines secreted by the adipose tissue may have pro-inflammatory functions and worsen both skin and joint disease in PsA.

A few studies have indicated that patients with obesity may be less likely to achieve remission. ^{16 17} Furthermore, weight reduction may improve the achievement of remission for those initiating biological therapies. ¹⁸ However, little is known on the effect of obesity on reaching remission/LDA when defined by indices and patients' opinion. In this study, we aimed to explore the association between obesity and remission/LDA when defined according to validated indices and patients' opinion, using an international clinic cohort.

METHODS

We used the baseline data of an international multicentre study performed in 2018, Remission/Flare in PsA (ReFlaP; NCT03119805). ReFlaP recruited adult patients with physician diagnosed PsA from 21 centres in 14 countries (Austria, Brazil, Canada, Estonia, France, Germany, Italy, Romania, Russia, Singapore, Spain, Turkey, United Kingdom and USA). We recruited patients with at least 2 years' disease duration, as they should have a more comprehensive experience of disease flare or remission.

Data collection

We collected demographic data, including age, sex, years of schooling, current use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and/or biologic (b-)DMARDs. Clinical data collected included 66/68 swollen/tender joint counts, enthesitis (Leeds Enthesitis Index) and C reactive protein (CRP).

Comorbidities were collected using the Functional Comorbidity Index (FCI), which comprises 17 additional conditions on top of arthritis. ¹⁹ Recent data have demonstrated preliminary data on construct validity²⁰ and known group validity²¹ of FCI in PsA.

PROs included pain (in numeric rating scale, NRS 0–10, none to worst), PGA of disease activity (NRS 0–10, none to worst), Health Assessment Questionnaire-disability index (HAQ-DI) and Psoriatic Arthritis Impact of Disease-12 (PsAID-12).

Defining remission

Three remission criteria were used in this study.

- Remission by Disease Activity index for PSoriatic Arthritis (DAPSA-REM). DAPSA is a measure of peripheral arthritis activity with summation of tender joint count (0–68), swollen joint count (0–66), pain, PGA and CRP.²² A cut-off value of ≤4 was considered as DAPSA-REM; >4 and ≤14 as LDA; >14 and ≤28 as moderate disease activity and >28 as high disease activity.²³
- 2. VLDA, defined as the presence of these seven items: tender Joint count ≤1; swollen joint count ≤1; enthesitis count ≤1; PGA ≤2/10; pain ≤1.5/10; skin psoriasis (PASI ≤1 or BSA ≤3%) and HAQ-DI ≤0.5.²⁴
- 3. Remission by patients' opinion. We asked patients to answer yes/no to this question: at this time, is your PsA in remission, if this means: you feel your disease is as good as gone? This phrasing of this remission criteria was developed with input from four patient research partners with PsA and based on previous work in remission criteria in rheumatoid arthritis. We previously reported moderate agreement of remission by patients' opinion and PGA ≤1 (Kappa 0.43). 10

LDA data were collected using (1) MDA defined as having at least 5/7 items in VLDA criteria (including VLDA); (2) DAPSA-LDA (inclusive of DAPSA-REM), defined as DAPSA ≤14; and finally, (3) LDA by patients' opinion, by patients answering 'yes' to this question: 'at this time, are you in LDA, if this means: your disease is in low activity but it is not as good as gone?'

Obesity

Obesity information was collected by two methods. First, body weight and height were measured at recruitment to calculate the body mass index (BMI) in kg/m². Second, comorbidities were collected by the attending physician as yes/no answers in the FCI obesity item. ¹⁹ Obesity in the current study was defined as a 'yes' answer to FCI obesity item and/or measured BMI $\geq 30 \, \text{kg/m}^2$.

Statistical analysis

Patients with available data for remission (by indices and patients' opinion) were included in this analysis. Demographic and clinical variables were described as mean (SD) or frequencies for continuous or categorical variables as appropriate; comparisons were made between patients with obesity versus non-obese. No imputation

Table 1 Patient characteristics of psoriatic arthritis patients with/without obesity (n=431)

	Non-obese (n=295)	Obese (n=136)
Age, years	51.5 (13.1)	54.4 (11.0) *
Female, n (%)	125 (43.3)	84 (62.2) **
Schooling, years	12.5 (4.2)	11.7 (4.6)
Duration of PsA, years	11.1 (8.3)	10.5 (7.8)
Number of other comorbidities (FCI), 0–17	1.6 (0.9)	2.4 (2.0) **
Current use of csDMARDs, n (%)	170 (61.2)	85 (66.9)
Current use of bDMARDs n (%)	173 (61.3)	76 (60.8)
Tender joints, 0-68	4.0 (8.4)	6.5 (11.7) *
Swollen joints, 0-66	2.5 (8.4)	1.7 (2.8)
Leeds enthesitis index, 0-6	0.5 (1.2)	0.9 (1.7) **
Psoriasis severity, n (%)		
No psoriasis/ limited psoriasis (<1-5%)	258 (91.8)	116 (88.6)
Extensive psoriasis (6-20%)	18 (6.4)	13 (9.9)
Very extensive psoriasis (>20)	5 (1.8)	2 (1.5)
CRP, mg/dL	1.2 (3.5)	2.3 (8.1) *
Pain, 0-10	3.8 (2.7)	4.8 (2.8) **
PGA disease activity, 0-10	2.9 (2.5)	3.5 (2.5) *
HAQ-DI, 0-3	0.5 (0.6)	0.9 (0.7) **
DAPSA	15.2 (17.0)	19.9 (18.0) *
PsAID-12, 0-10	3.0 (2.3)	4.1 (2.6) **
Pain, 0-10	3.7 (2.8)	4.7 (2.8) **
Skin, 0-10	2.5 (2.7)	3.0 (2.9)
Fatigue, 0-10	3.9 (3.0)	4.8 (3.2) **
Work or leisure activities, 0-10	3.3 (3.0)	4.8 (3.26) **
Functional capacity, 0-10	3.3 (2.9)	4.5 (3.2) **
Discomfort, 0-10	3.4 (2.9)	4.6 (3.0) **
Sleep, 0-10	2.9 (3.1)	4.1 (3.4) **
Anxiety, 0–10	2.8 (3.0)	3.5 (3.3) *
Coping, 0-10	2.5 (2.6)	3.4 (3.0) **
Embarrassment, 0-10	1.8 (2.7)	2.8 (3.3) **
Social participation, 0-10	2.1 (2.9)	3.0 (3.3) **
Depression, 0-10	1.9 (2.7)	2.9 (3.3) **

Mean (SD) shown unless specified otherwise. *p<0.05; **p<0.01 for comparisons between non-obese and obese groups. bDMARDs, biological disease modifying anti-rheumatic drugs; CRP, C reactive protein; csDMARDs, conventional synthetic disease modifying anti-rheumatic drugs; DAPSA, Disease Activity in PSoriatic Arthritis; FCI, Functional Comorbidity Index; HAQ-DI, Health Assessment Questionnaire Disability Index: LDA, low disease activity: PGA, patient global assessment of disease activity; PsA, psoriatic arthritis; PsAID, Psoriatic Arthritis Impact of Disease.

of missing data was performed; data were analysed on complete cases.

We compared the rates of obesity according to each remission/LDA definition. We constructed generalised linear models (binary logistic type), for the outcome variables, that is, the three remission/LDA definitions. In

addition to obesity, variables that were not components of remission criteria were considered to be included as adjustment variables, that is, age, sex, years of schooling, duration of PsA, use of current cs/b-DMARDs and other comorbidities. These variables were chosen as they have previously been reported to be associated with remission in PsA. 16 17 26 Comorbidities other than obesity were considered using the FCI without the obesity category to avoid circularity. Although disease activity variables were the major contributor of remission/LDA as we previously reported, 26 we did not consider them in analysis models as they are the components of remission/LDA definitions. Variables associated with remission/LDA outcomes with p value ≤0.10 in the univariable models were included in the multivariable logistic regression models. As female sex is known to be associated with remission/LDA,²⁷ we explored the interaction of sex and obesity in exploratory models. A sensitivity analysis limiting to patients with available data for BMI was performed, with obesity defined by measured BMI $\geq 30 \text{ kg/m}^2$. Finally, we further explored the odds of the presence of each component of VLDA in obese versus non-obese patients with adjustment on age and sex.

Statistical analyses were conducted using IBM SPSS Statistics for Windows, V.25 (IBM, Armonk, New York). All reported p values were two sided, and p values less than 0.05 were considered statistically significant.

RESULTS

Overall, 431 patients were analysed. The mean (SD) age was 52.4 (12.6) years, 49.3% were women.

Overall, 136 (31.6%) patients were obese defined as either BMI $\geq 30 \text{ kg/m}^2$ or affirmed as obesity in FCI. Thirty-seven (8.6%) participants had missing data for either weight or height for the computation of BMI. Among patients classified as obese according to FCI, 7 out of 70 participants (10%) had BMI $<30 \text{kg/m}^2$. Among the non-obese cases according to the FCI, 54 out of 324 participants (16.7%) had their measured BMI ≥30 kg/m². The 136 patients defined here as obese were older, more frequently woman and had a higher number of other comorbidities compared with those who were non-obese (table 1). Compared with non-obese patients, patients with obesity had higher tender joint counts, enthesitis scores and CRP, but not swollen joint counts. In addition, PROs were significantly worse among patients with obesity than those without, including higher pain score, worse PGA, worse physical function by HAQ-DI and worse HR-QoL in all PsAID domains except skin (table 1). Rates of obesity by country are shown in online supplemental table 1.

Remission/LDA

Congruent with our previous report, 19.5%, 14.8% and 22.7% of patients reached remission by DAPSA-REM, VLDA and patients' opinion, respectively, while 56.4%, 51.8% and 60.2% reached LDA by DAPSA-LDA, MDA

and patients' opinion. Patient characteristics stratified by remission/LDA criteria are shown in online supplemental tables 2 and 3. Patients not having remission/LDA by indices were more frequently women, had higher number of comorbidities and had higher BMI. Demographics of patients by remission/LDA indices and patients' opinion are shown in online supplemental tables 2 and 3.

Association between obesity and remission/LDA

The respective unadjusted rates for remission by DAPSA-REM, VLDA and patients' opinion in patients with obesity compared with non-obese were 8.8% vs 24.4% (p <0.001), 5.1% vs 19.3% (p<0.001) and 22.1% vs 23.1 (p=0.90). The respective rates for LDA by DAPSA-LDA, MDA and patients' opinion were 47.8% vs 60.3% (p=0.0016), 37.5% vs 55.3% (p<0.001) and 61.2% vs 68.1% (p=0.187). Thus, there was a statistically significantly lower proportion of patients with obesity who were in remission by VLDA and DAPSA, but there was no difference in remission from the patients' opinion (figure 1A). A similar pattern was seen for LDA states and patients' opinions (figure 1B).

In the univariable model, obesity, female sex, current DMARD use and higher number of other comorbidities were associated with lower odds of being in remission by VLDA (online supplemental table 4). Obesity, female sex, longer duration of PsA and higher number of other comorbidities were associated with lower odds of DAPSA-REM. The associations between obesity and all models on remission/ LDA are summarised in table 2. The detail of statistical analysis of each remission/ LDA status in each model is given in online supplemental tables 4–9.

In the multivariable model, obesity was statistically significantly associated with lower odds of DAPSA-REM, after adjustment for age, sex, use of b/cs-DMARDs and other comorbidities (OR 0.39; 95% CI 0.19 to 0.80; p=0.009) (table 2 and online supplemental table 4). Similarly, obesity remained statistically significantly associated with lower odds of VLDA after adjustments (table 2 and online supplemental table 1). Patients with obesity were three times less likely than those without to be in VLDA (OR 0.31; 95% CI 0.13 to 0.77; p=0.011). However, obesity was not associated with remission by patients' opinion (table 2 and online supplemental table 6). Obesity was associated with MDA in both univariable and multivariable adjustment models (online supplemental table 7); the association of obesity and DAPSA-LDA was lost in the multivariable model (online supplemental table 8).

In the exploratory model, we did not observe a significant interaction term between sex and obesity, p for interaction were 1.00 and 0.21, respectively, for VLDA and DAPSA-REM models. Results of sensitivity analysis limiting to patients with BMI data and obesity defined as BMI $\geq 30 \, \text{kg/m}^2$ were generally consistent (online supplemental table 10).

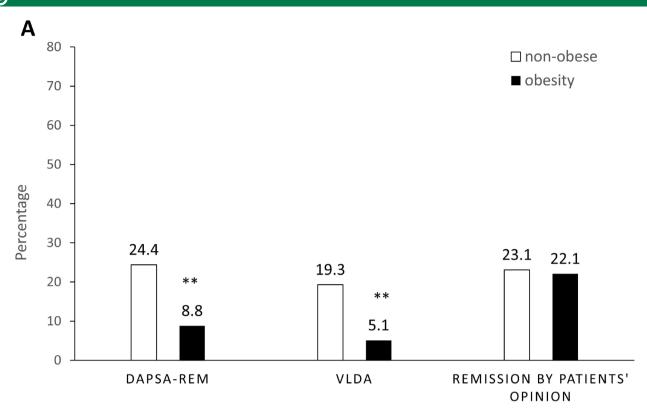
For VLDA components, the odds of being in low pain level and good functional outcomes were lower in obese patients versus non-obese, which remained statistically significant after adjustment with age and sex (table 3).

DISCUSSION

In this multicentre international sample of patients with established PsA, we found that patients with comorbid obesity had lower odds of being in remission/LDA defined by different indices, after adjustment for multiple other variables. Patients with obesity were 2.5–3 times less likely than their non-obese counterparts to be in DAPSA remission and VLDA; and 1.6 times less likely to be in MDA. However, the rates of remission by patients' opinion and the rates of DAPSA-LDA (defined as DAPSA \leq 14) were similar comparing patients with or without comorbid obesity in the multivariable-adjusted models. Compared with non-obese patients, low pain levels and good physical function were the most difficult components to be among the VDLA components, for obese patients.

Obesity is prevalent among patients with PsA and associated with higher disease activity, worse disease impact^{16 17} and possibly poorer response to treatment.²⁸ Obesity represents a state of low-grade systemic inflammation, and elevated CRP has been repeatedly described across different population, across sex and age groups.²⁹ Adipokines secreted by adipose tissue are increasingly recognised to regulate various immune responses. For instances, the most described adipokine, leptin, promotes pro-inflammatory signals including interleukin (IL) -1α , IL-17 and tumour necrosis factor (TNF)-α.³⁰ It has been reported that PsA patients who are obese may have higher disease activity and poorer response to treatment. PsA patients who were obese had higher disease burden measured by PsAID and Routine Assessment of Patient Index Data (RAPID3).31 In a longitudinal cohort, PsA patients with obesity had a lower probability of achieving sustained MDA. ¹⁶ Among patients initiating TNF inhibitor treatment, obesity was a strong predictor of not achieving Clinical Disease Activity Index remission, 17 while weight loss was associated with a higher rate of achieving MDA.³² Our study findings generally expand those reported in the literature. CRP levels among our patients with obese were two times as high as those without. Once again, we observe that obesity is associated with higher pain scores, and worse physical function and HR-QoL. In addition, we showed that patients with comorbid obesity also had lower probability to be in remission. This highlights the importance of recognising and managing obesity as an important comorbidity to improve the care of patients with PsA.

Despite the lack of consensus in the instruments to define remission, achieving remission is a desirable target in the care of patients with PsA.⁴ Several index-based criteria for remission have been developed and demonstrated their ability to predict less radiographic damage among patients achieving them.⁶ 11 33 This theoretically



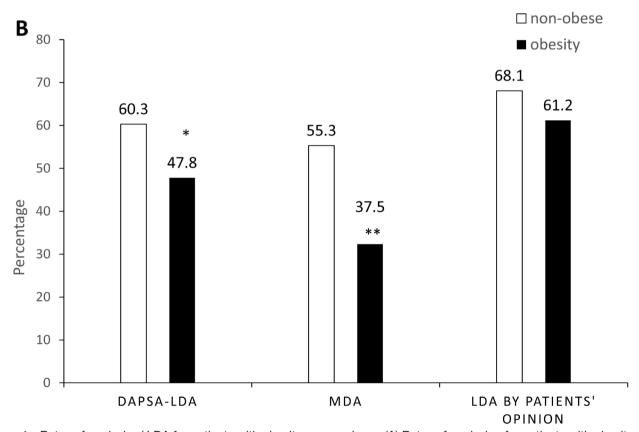


Figure 1 Rates of remission/ LDA for patients with obesity vs non-obese. (A) Rates of remission for patients with obesity vs non-obese. (B) Rates of low disease activity for patients with obesity vs non-obese. *Unadjusted p<0.05; **Unadjusted p<0.001; DAPSA-LDA, Low disease activity by Disease Activity in Psoriatic Arthritis; DAPSA-REM, Remission by Disease Activity in Psoriatic Arthritis; LDA, low disease activity state; MDA, minimal disease activity; VLDA, very low disease activity.

Table 2 Summary of odds to be in remission/LDA comparing patients with obesity versus non-obese

	Univariable model		Multivariable model*	
	OR (95% CI)	Р	OR (95% CI)	Р
Remission				
DAPSA-REM	0.32 (0.16, 0.62)	0.001	0.39 (0.19, 0.80)	0.009
VLDA	0.23 (0.10, 0.55)	0.001	0.31 (0.13, 0.77)	0.011
Remission by patients' opinion	0.869 (0.504, 1.497)	0.613	_	-
LDA				
DAPSA-LDA	0.448 (0.263, 0.762)	0.003	0.728 (0.446, 1.187)	0.203
MDA	0.50 (0.31, 0.78)	0.002	0.61 (0.38, 0.99)	0.045
LDA by patients' opinion	0.80 (0.51, 1.26)	0.333	-	-

Bold: variables statistically significantly associated with remission/ LDA of interest.

should lead to better quality of life for patients with PsA. Yet, what patients perceive as 'good status' is less studied. We previously explored clusters of factors associated with remission and LDA in patients' opinion and found that apart from disease impact and disease activity in different domains, chronicity/age and comorbidities were the key contributing factors.²⁶ Using the same data set, we have also reported that there was only moderate agreement between patient-perceived remission and remission defined by VLDA (Kappa 0.65) or DAPSA (Kappa 0.60). Close to half of patients in self-perceived remission were not in VLDA or DAPSA remission, while a third of those in self-perceived LDA were not considered in LDA by index-based measures. ¹⁰ In the current study, we further revealed that one of the key comorbidities, obesity was associated with high disease impact by indices on patients with PsA. However, we did not observe a statistically significant association between obesity and remission

according to patients' opinion. Obese patients reported higher disease impact but despite this they also reported that their disease was controlled. The reasons behind this are unclear. Possible reasons include overestimating swollen joints in obese patients, higher articular damage in obesity due to osteoarthritis and influences from other comorbidities. While numerous studies in the general population have reported associations between obesity and chronic pain, reduced physical activity and pain sensitisation,³⁴ the mechanism underlying this observation is elusive. Mechanical, behavioural and psychological factors may play a role that requires further studies.

Exploring the individual components within VLDA, obese patients were less likely to have a low pain score and good physical function compared with non-obese. Whether obese patients may have a less stringent threshold to endorse remission requires more study. The same is true for potential psychological factors such as

 Table 3
 Association between obesity and probability of each component in MDA

	Univariable model		Multivariable model *	
	OR (95% CI)	Р	OR (95% CI)	Р
Tender joint count≤1	0.62 (0.41, 0.93)	0.021	0.71 (0.45, 1.13)	0.152
Swollen joint count≤1	0.73 (0.47, 1.13)	0.154	0.78 (0.48, 1.28)	0.328
PASI≤1 or BSA≤3%	0.68 (0.34, 1.35)	0.274	0.55 (0.25, 1.18)	0.123
HAQ≤0.5	0.39 (0.26, 0.60)	<0.001	0.52 (0.32, 0.83)	0.007
Pain≤1	0.40 (0.23, 0.69)	0.001	0.50 (0.27, 0.91)	0.023
PGA≤2	0.63 (0.42, 0.95)	0.027	0.81 (0.51, 1.28)	0.369
Tender entheseal site≤1	0.54 (0.31, 0.94)	0.030	0.64 (0.33, 1.23)	0.635

Bold: statistically significant.

bDMARDs, biological disease modifying anti-rheumatic drugs; BSA, body surface area; csDMARDs, conventional synthetic disease modifying anti-rheumatic drugs; DAPSA, Disease Activity in PSoriatic Arthritis; FCI, Functional comorbidity index; HAQ, Health Assessment Questionnaire; LDA, low disease activity status; PASI, Psoriasis Area and Severity Index; PGA, patient global assessment.

^{*}List of adjustment variables considered were age, sex, years of schooling, duration of PsA, current use of cDMARDs, current use of bDMARDs and other comorbidities in FCI. Variables adjusted in each multivariable model were chosen from those with significant p<0.1 in univariable model as detailed in online supplemental tables 4–8.

bDMARDs, biological disease modifying anti-rheumatic drugs; csDMARDs, conventional synthetic disease modifying anti-rheumatic drugs; DAPSA, Disease Activity in PSoriatic Arthritis; FCI, Functional Comorbidity Index; LDA, low disease activity status; REM, remission; VLDA, very low disease activity; vs, versus.

^{*}Regression model adjusted with age and sex.

expectations of the target of good status that they could achieve, and how much symptoms patients may attribute to PsA or their comorbidities including obesity.³⁵ Equally, the benefit of remission versus LDA in this patient population needs to be clarified. Results from this study support a recommendation to manage obesity in PsA with the hope to facilitate more successful T2T treatment and to decrease symptoms and life impact burden. The key message for physicians and healthcare providers is the awareness of the importance of shared decision-making when discussing the impact of obesity on expected treatment outcomes and the implications for disease management. For instance, higher BMI may adversely affect the volume of drug distribution, leading to insufficient dosing and reduced efficacy, particularly for TNF blockers.^{28 36} Currently, infliximab, golimumab and ustekinumab can be given as weight-based regimen, while other biologics are usually given in fixed doses.³⁷ In addition to emphasis on weight reduction, adjustment of dosing of therapeutics may be considered for individual patients.

We acknowledge several limitations of our study. First, patients were recruited from tertiary referral centres and results may not be generalisable to milder PsA. The crosssectional analysis does not allow study on changes in remission status or causality. Although we collected data for one follow-up visit, the small sample size precluded longitudinal analysis. Data from this study do not preclude obese patients having high disease activity and impact at baseline, and still have good potential to improve and be satisfied with T2T strategy overtime. We may not be able to account for variables we did not collect, such as fibromyalgia, which could be an important interaction with obesity in the models. Comorbidities in this study were collected through FCI, which was developed to predict functional outcomes rather than mortality. 19 Finally, obesity was defined based on either BMI or physician report, which led to some discrepancies.

In conclusion, PsA patients with concurrent obesity had lower odds of being in remission by indices, highlighting the importance of managing obesity to improve the care of patients with PsA. Shared decision-making is important for an individualised target of management.

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Acknowledgements The ReFlap study was funded by Pfizer through an investigator-initiated research grant. Pfizer played no role in the study itself and did not have access to the analyses or the paper prior to publication. YYL is supported by the Singapore National Medical Research Council. LCC is supported by the National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. We acknowledge the support of the National Institute for Health Research Clinical Research Network (NIHR CRN).

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Contributors Substantial contributions to study conception and design: YYL, LCC, MdW, JSS, A-MO, LG; substantial contributions to analysis and interpretation of the data: YYL, LE, A-MO, LCC, MdW, JSS, UtK, PP, JDC, RS, AB, ED, SM, MS, UmK, LG; drafting the article or revising it critically for important intellectual content: YYL, LE, A-MO, LCC, MdW, JS, UtK, PP, JDC, RS, AB, ED, SM, MS, UmK, LG; LG; final approval of the version of the article to be published: YYL, LE, A-MO, LCC, MdW, JSS, UtK, PP, JDC, RS, AB, ED, SM, MS, UmK, LG; Guarantor of the work: LG.

Funding This work is supported by Pfizer through an investigator-initiated research grant: Project WI224950. These are infrastructure grants to LCC without specific numbers. They have no direct expendable support to this project, BRC. Clinical Research Network, Department of Health and Social Care, National Institute for Health and Care Research, National Institute for Health Research (NIHR), NIHR, Oxford Biomedical Research.

Competing interests YYL has received consulting fee and speaking fees from AbbVie, DKSH, Janssen, Novartis and Pfizer. LCC is an Editorial Board Member of RMD Open, she has received grants/research support from AbbVie, Amgen, Celgene, Eli Lilly, Janssen, Novartis, Pfizer and UCB; worked as a paid consultant for AbbVie, Amgen, Bristol Myers Squibb, Celgene, Eli Lilly, Gilead, Galapagos, Janssen, Moonlake, Novartis, Pfizer and UCB; and has been paid as a speaker for AbbVie, Amgen, Biogen, Celgene, Eli Lilly, Galapagos, Gilead, GSK, Janssen, Medac, Novartis. Pfizer and UCB. MdW has received fees for lectures or consultancy from Celgene, Eli Lilly, Pfizer and UCB. JSS received Research Grants for his institution from Abbvie, AstraZeneca, Lilly, Novartis and Roche, and honoraria for consultancies and/or speaking engagements from AbbVie, Amgen, AstraZeneca, Astro, Bristol-Myers Squibb, Celgene, Celltrion, Chugai, Lilly, Merck Sharp & Dohme, Novartis- Sandoz, Pfizer, R-Pharm, Samsung, Sanofi, and UCB. UK has received grants and research support and consultancy fees from AbbVie, Amgen, Biocad, Biogen, Chugai, Eli Lilly, Fresenius, Gilead, Grünenthal, GSK, Hexal, Janssen, MSD, Novartis, onkowoessen.de, Pfizer, Roche, UCB and Viatris. AB has received speakers' fees and consulting fees from Abbvie, Amgen, Akros, Astra-Zeneca, Angellini, AlphaSigma, BMS, Berlin-Chemie, Biogen, Lilly, Mylan, MSD, Novartis, Pfizer, Roche, Sandoz, Teva, UCB, Zentiva; and was investigator in clinical trials sponsored by Akros, MSD, Sanofi, Pfizer, Astra-Zeneca, Novartis, BMS, GSK, Roche, UCB, Sandoz. LG has received research grants from Sandoz, UCB; consulting fees from AbbVie, Amgen, BMS, Celltrion, Galapagos, Janssen, Lilly, MSD, Novartis, Pfizer, Sandoz, UCB.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Ethics approval was sought and obtained in each country or centre. Prior to participation, all patients signed informed consent. Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

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REFERENCES

- 1 FitzGerald O, Ogdie A, Chandran V, et al. Psoriatic arthritis. Nat Rev Dis Primers 2021;7:59.
- 2 Orbai A-M, de Wit M, Mease PJ, et al. Updating the psoriatic arthritis (PsA) core domain set: a report from the PsA workshop at OMERACT 2016. J Rheumatol 2017;44:1522–8.
- 3 Gudu T, Gossec L. Quality of life in psoriatic arthritis. Expert Rev Clin Immunol 2018;14:405–17.
- 4 Smolen JS, Schöls M, Braun J, et al. Treating axial spondyloarthritis and peripheral spondyloarthritis, especially psoriatic arthritis, to target: 2017 update of recommendations by an international task force. Ann Rheum Dis 2018;77:3–17.
- 5 Gossec L, Baraliakos X, Kerschbaumer A, et al. EULAR recommendations for the management of psoriatic arthritis with pharmacological therapies: 2019 update. Ann Rheum Dis 2020;79:700–12.
- 6 Kavanaugh A, van der Heijde D, Beutler A, et al. Radiographic progression of patients with psoriatic arthritis who achieve minimal disease activity in response to golimumab therapy: results through 5 years of a randomized, placebo-controlled study. Arthritis Care Res (Hoboken) 2016;68:267–74.
- 7 Cheng IT, Shang Q, Li EK, et al. Effect of achieving minimal disease activity on the progression of subclinical atherosclerosis and arterial stiffness: a prospective cohort study in psoriatic arthritis. Arthritis Rheumatol 2019;71:271–80.
- 8 Aouad K, Moysidou G, Rakotozafiarison A, et al. Outcome measures used in psoriatic arthritis registries and cohorts: a systematic literature review of 27 registries or 16,183 patients. Semin Arthritis Rheum 2021;51:888–94.
- 9 Hagège B, Tan E, Gayraud M, et al. Remission and low disease activity in psoriatic arthritis publications: a systematic literature review with meta-analysis. Rheumatology (Oxford) 2020;59:1818–25.
- 10 Gorlier C, Orbai A-M, Puyraimond-Zennmour D, et al. Comparing patient-perceived and physician-perceived remission and low disease activity in psoriatic arthritis: an analysis of 410 patients from 14 countries. Ann Rheum Dis 2019;78:201–8.
- 11 Coates LC, Nash P, Kvien TK, et al. Comparison of remission and low disease activity states with DAPSA, MDA and VLDA in a clinical trial setting in psoriatic arthritis patients: 2-year results from the FUTURE 2 study. Semin Arthritis Rheum 2020;50:709–18.
- 12 Kumthekar A, Ogdie A. Obesity and psoriatic arthritis: a narrative review. Rheumatol Ther 2020;7:447–56.
- 13 Kumar S, Han J, Li T, et al. Obesity, waist circumference, weight change and the risk of psoriasis in US women. J Eur Acad Dermatol Venereol 2013;27:1293–8.

- 14 Setty AR, Curhan G, Choi HK. Obesity, waist circumference, weight change, and the risk of psoriasis in women: nurses' health study II. Arch Intern Med 2007;167:1670–5.
- 15 Love TJ, Zhu Y, Zhang Y, et al. Obesity and the risk of psoriatic arthritis: a population-based study. Ann Rheum Dis 2012;71:1273–7.
- 16 Eder L, Thavaneswaran A, Chandran V, et al. 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.
- 17 Ogdie A, Palmer JL, Greenberg J, et al. Predictors of achieving remission among patients with psoriatic arthritis initiating a tumor necrosis factor inhibitor. J Rheumatol 2019;46:475–82.
- 18 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.
- 19 Groll DL, To T, Bombardier C, et al. The development of a comorbidity index with physical function as the outcome. J Clin Epidemiol 2005;58:595–602.
- 20 Popescu ND, Dima A, Berza IA, et al. AB0954 concordance between different comorbidities scores in patients with psoriatic arthritis. Ann Rheum Dis 2022;81:1605–6.
- 21 Perrotta FM, Scriffignano S, Ciccia F, et al. Clinical characteristics of potential "difficult-to-treat" patients with psoriatic arthritis: a retrospective analysis of a longitudinal cohort. Rheumatol Ther 2022;9:1193–201.
- 22 Schoels M, Aletaha D, Funovits J, et al. Application of the DAREA/ DAPSA score for assessment of disease activity in psoriatic arthritis. Ann Rheum Dis 2010;69:1441–7.
- 23 Schoels MM, Aletaha D, Alasti F, et al. Disease activity in psoriatic arthritis (PsA): defining remission and treatment success using the DAPSA score. Ann Rheum Dis 2016;75:811–8.
- 24 Coates LC, Fransen J, Helliwell PS. Defining minimal disease activity in psoriatic arthritis: a proposed objective target for treatment. *Ann Rheum Dis* 2010;69:48–53.
- Rasch LA, Boers M, Hill CL, et al. Validating rheumatoid arthritis remission using the patients' perspective: results from a special interest group at OMERACT 2016. J Rheumatol 2017;44:1889–93.
- 26 Coates LC, Robinson DE, Orbai A-M, et al. What influences patients' opinion of remission and low disease activity in psoriatic arthritis? Principal component analysis of an international study. Rheumatology (Oxford) 2021;60:5292–9.
- 27 Orbai A-M, Perin J, Gorlier C, et al. Determinants of patient-reported psoriatic arthritis impact of disease: an analysis of the association with sex in 458 patients from fourteen countries. Arthritis Care Res (Hoboken) 2020;72:1772–9.
- 28 Gratacós J, Galíndez E, Otón T. Is obesity a predictor for lack of response to treatment in psoriatic arthritis? A systematic review. *Reumatol Clin (Engl Ed)* 2021;17:268–78.
- 29 Choi J, Joseph L, Pilote L. Obesity and C-reactive protein in various populations: a systematic review and meta-analysis. *Obes Rev* 2013;14:232–44.
- 30 likuni N, Lam QLK, Lu L, et al. Leptin and inflammation. Curr Immunol Rev 2008;4:70–9.
- 31 Walsh JA, Wan MT, Willinger C, et al. Measuring outcomes in psoriatic arthritis: comparing routine assessment of patient index data and psoriatic arthritis impact of disease. J Rheumatol 2020;47:1496–505.
- 32 Di Minno MND, Peluso R, Iervolino S, et al. Weight loss and achievement of minimal disease activity in patients with psoriatic arthritis starting treatment with tumour necrosis factor a blockers. Ann Rheum Dis 2014;73:1157–62.
- 33 Coates LC, Helliwell PS. Validation of minimal disease activity criteria for psoriatic arthritis using interventional trial data. Arthritis Care Res (Hoboken) 2010;62:965–9.
- 34 Chin S-H, Huang W-L, Akter S, et al. Obesity and pain: a systematic review. Int J Obes (Lond) 2020;44:969–79.
- 35 Walsh JA, Ogdie A, Michaud K, et al. Impact of key manifestations of psoriatic arthritis on patient quality of life, functional status, and work productivity: findings from a real-world study in the United States and Europe. *Joint Bone Spine* 2023;90:105534.
- 36 Singh S, Facciorusso A, Singh AG, et al. Obesity and response to anti-tumor necrosis factor-a agents in patients with select immunemediated inflammatory diseases: a systematic review and metaanalysis. PLoS One 2018;13:e0195123.
- 37 Coates L, Gossec L. The updated GRAPPA and EULAR recommendations for the management of psoriatic arthritis: similarities and differences. *Joint Bone Spine* 2023;90:105469.