PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	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
AUTHORS	Vallejo-Yagüe, Enriqueta; Burkard, Theresa; Micheroli, Raphael; Burden, Andrea

VERSION 1 – REVIEW

REVIEWER	Queiro, Ruben Department of Rheumatology, HU, Central de Asturias
REVIEW RETURNED	27-Feb-2022

GENERAL COMMENTS	In this work, the authors emphasize the idea that obesity is associated with worse clinical outcomes and less possibility of achieving treatment goals in PsA, such as the MDA or the DAPSA response. Although the study is methodologically correct, it adds little to what we already know about this topic. In a recent systematic review with meta-analysis of 54 cohorts including 19,372 patients with IMIDs treated with anti-TNFα agents, obesity was associated with 60% higher odds of failing anti-TNFα therapy as compared to non-obese and normal BMI subjects, for most IMIDs, including RA, axial SpA, psoriasis, and PsA (PLoS One. 2018;13:e0195123). Some aspects to consider are: The time frame of the observation starts in 1997 when biological therapies for PsA were hardly available (the first was approved in 2002) and there were no ts-DMARDS. Could the authors comment on this? Why hasn't a time frame been chosen that corresponds to when these therapies could actually be used (eg from 2002)? On the other hand, no mention is made of whether standardized criteria were used to classify the disease. Before 2006, the standards were those of Moll and Wright (others also existed, although less used), and from that date, most studies on PsA use the CASPAR criteria. You don't mention any of this. Although in your introduction you point out that there is still controversy in the association between obesity and clinical outcomes in PsA, the vast majority of publications really go in the same direction, so there is little room for controversy on this topic. See again PLoS One. 2018;13:e0195123. Given such a wide observation window in your country's registry, why have you only considered the outcomes of your study at 12 months? What do we know about the information at 2 or 3 years? The cutaneous criterion within the MDA response is explicit (PASI or BSA) not just the clinician's opinion on this disease domain. Although your study refers to biological or ts-DMARDS, the numbers you provide are, by far, referred to TNFi. I think you

	should comment on this in your methods and/or discussion. This becomes relevant since the negative effect of obesity on TNFi persistence does not seem to be as important when other therapeutic routes are analysed, such as IL-17A inhibitors (Expert Opin Biol Ther. 2021 Dec;21(12):1539-1541) Your explanation as to why there is a disconnect between outcomes in terms of MDA or DAPSA remission and persistence of treatment is not very convincing. In fact, most clinicians are not usually inclined to prolong therapies in obese PsA patients who do not achieve treatment goals, but rather to seek alternative therapeutic routes to that of TNFi. In general, a non-response in the first 3-4 months of treatment usually leads to a change of treatment in routine clinical practice. Finally, as you rightly point out, the concept of remission is an evolving concept in the field of PsA, and more and more attention is being paid to the opinion of patients. In obese subjects, etiopathogenic aspects (already mentioned by you) surely coincide, along with others of a diverse nature, which ultimately have an influence on the way in which the patient experiences his/her disease, and which determine those remission rates that you observe, as well as the rate of therapeutic successes and failures. Perhaps you should reflect on this in your discussion.

REVIEWER	Glintborg, B. Rigshosp
REVIEW RETURNED	02-Mar-2022

GENERAL COMMENTS	This manuscript have several aims – mainly to explore b/tsDMARD treatment outcomes according to body mass index/obesity upon treatment start, but also to explore overlaps between a variety of treatment outcomes in PsA. The manuscript is based on data from the wellknown SCQM registry, but does not seem to have a rheumatologist in the author group. Although the manuscript is fairly well written, it also seems overly complicated and focusing on a clinical situation that is already well described. The only study that the authors bring forward illustrating conflicting previous results regarding the negative impact of obesity is 2013 (ref 17) including only 135 patients and likely having low power. First and foremost, I suggest the authors to reconsider the presentation of knowledge gap and to rephrase accordingly. I have a line of additional comments: It seems an important result is that obesity and overweight was frequent in the studied population. Could that be a result to be reported more clearly? The authors wonder if patients with underweight should not have been included in the normal weight group. Could a sensitivity analyses excluding these patients be performed? Title: Suggest to more clearly state that patients starting first b/tsDMARD were included Abstract: The conclusion should include all aims put forward, also the overlapping of study outcomes. I wonder why the authors use the phrase ‘accordance’ – without explaining the difference between accordance and overlap? Strengths and limitations: The authors state that the source used was optimal – without explaining why. However, only half of patients had complete data

	and imputation was needed. Suggest to phrase in a more objective manner. The current strengths and limitations appear unstructured – with a mixture of statements, limitations and study descriptions. Suggest to rephrase in a more stringent and structured (and briefer?) manner Methods: This whole study is based on a single measurement of weight and height. Did the authors consider the validity of these measurements – e.g. were they measured or selfreported by the patients themselves? Main outcome was MDA within first year. What was the time-window for evaluating this outcome – and how was early withdrawal handled? The authors put forward a line of co-variates. But I miss a definition of these – e.g. how was low education defined? What inflammatory markers were included (CRP?), was the joint count based on 28 or 66 joints? How was comorbidities evaluated – selfreported by patient, in patient files? According to mediciation use? The authors put forward the term 'fragility', how was this evaluated? Data analyses: The DAG diagram seems interesting, why was comorbidities (in text and figure) and education (in text) not mentioned/included? It seems as if treatment retention during one year of follow-up was evaluated as a yes-no outcome instead of a traditional time to event analysis which could be better use of the data available and which also could include censoring/lack of followup in a meaningful way. What was the reason for this decision? Patient and public involvement It is unfortunate that patients were not involved – or a rheumatologist? Please comment? Table 1: Please indicate what comparison p-value refers to – especially the p-value in the right column (compared to normal weight?) What is the scale for global skin manifestation? Figure 1, Supplementary Table S2, S3 The authors use the terminology 'n events', does this refer to patients achieving the outcome? Suggest to show not only events but also total number in group? Supplementary Figure S2 Please describe meaning of the colors shown and the scale used in the right side of Figure Supplementary Figure S4 There seem to be blue, grey and white nodes, and there to be filled and dotted lines. Please explain all details. Supplementary Figure S5 The interesting patient group excluded are those that were eligible for inclusion (PsA, b/tsDMARD treatment, age >18 and correct time period) BUT did not have data on weight and height. Suggest to restructure the figure accordingly.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1 Comments
Reviewer 1: Dr. Ruben Queiro, Department of Rheumatology, HU, Central de Asturias Competing interests of Reviewer: No competing interests

➢ Reviewer 1, comment #1
In this work, the authors emphasize the idea that obesity is associated with worse clinical outcomes and less possibility of achieving treatment goals in PsA, such as the MDA or the DAPSA response. Although the study is methodologically correct, it adds little to what we already know about this topic. In a recent systematic review with meta-analysis of 54 cohorts including 19,372 patients with IMIDs treated with anti-TNFα agents, obesity was associated with 60% higher odds of failing antiTNFα therapy as compared to non-obese and normal BMI subjects, for most IMIDs, including RA, axial SpA, psoriasis, and PsA (PLoS One. 2018;13:e0195123).
Answer:
We would like to thank the reviewer for the careful review of our manuscript. We appreciate that every comment reflected constructive feedback and it was formulated with care and supported with the appropriate reasoning and references. Thank you for improving our manuscript.
We agree on the high relevance of the systematic review by Singh S. and colleagues, 2018 (PLoS One
2018; 13: e0195123), which we cited in the article (ref. #16). Among the 20 randomized clinical trials (RCTs) and 34 observational studies included by Singh S. et al., only one RCT and 8 observational cohorts were psoriatic arthritis (PsA) studies (including those with and without psoriasis patients). Additionally, among the observational studies, most of them had relatively small sample size. For example, six had a sample size ≤330, and only one had a sample size bigger than ours (See Table 2 from Singh S. and colleagues 2018). Moreover, none were performed in the Swiss population, which may constitute a distinct population of interest due to their healthcare system, which differs from that of other European countries.
Thus, we trust that our study – including some patients treated with non-TNFi biologics – builds on top of existing evidence of the impact of obesity in patients with PsA, and it contributes to its growth. We have rephrased our introduction.
▪ Page 5, lines 85-92:
“Despite the growing evidence on the association between obesity and worse clinical response in PsA patients, most published observational cohort studies on this topic had relatively small sample size. For example, a systematic review investigating the association between obesity and response in immune-mediated inflammatory diseases identified one randomised clinical trial and eight observational cohort studies in PsA patients, but six of the included observational cohorts had a sample size ≤330 (Singh et al. 2018). Thus, further investigating this effect, especially in a different and bigger population cohort, remains of interest. Additionally, it is unclear whether the findings would remain consistent across outcome definitions.”

Reviewer 1, comment #2
Some aspects to consider are:
The time frame of the observation starts in 1997 when biological therapies for PsA were hardly available (the first was approved in 2002) and there were no ts-DMARDS. Could the authors comment on this? Why hasn't a time frame been chosen that corresponds to when these therapies could actually be used (eg from 2002)?
Answer:
The reviewer highlights here an interesting point. The earliest index date for our included population was 15.06.2000 (normal weight patient treated with etanercept). We could have restricted the study period to a specific time prior that. However, our methods described an unlimited look-back window for some of the baseline covariates (e.g., chronic comorbidities). Thus, we benefited from the earlier years of SCQM dataset to gather as much information as possible from those with early enrolment in the dataset.
Following the reviewer's point, while we decided to keep the study period as it was to gather as much information as possible (1997 to July 31st 2019), we modified the way the study population was described, including adult PsA patients who started their first biologic or targeted synthetic disease-modifying anti-rheumatic drug (b/tsDMARD) between June 1st 2020 and June 30th 2018.
▪ Page 5, lines 107-108:
"PsA patients (≥18 years old) starting their first b/tsDMARD in the SCQM registry between June 1st 2020 and June 30th 2018 (inclusive) were included in the study."

➢ Reviewer 1, comment #3
On the other hand, no mention is made of whether standardized criteria were used to classify the disease. Before 2006, the standards were those of Moll and Wright (others also existed, although less used), and from that date, most studies on PsA use the CASPAR criteria. You don't mention any of this.
Answer:
Thank you for this comment. In the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry, the diagnosis follows the physician's criteria. Thus, we can not assure that it follows any specific standardised criteria like the Moll and Wright or the CASPAR criteria. However, following the reviewer's comment, and understanding that this information belongs in the manuscript, we added it in our methods section.
▪ Page 5, line 105:
"Diagnosis of PsA is recorded in SCQM following the physician's criteria."

Reviewer 1, comment #4
Although in your introduction you point out that there is still controversy in the association between obesity and clinical outcomes in PsA, the vast majority of publications really go in the same direction, so there is little room for controversy on this topic. See again PLoS One. 2018;13:e0195123.
Answer:
We understand the point from the reviewer and agree that 'controversy' may have not been the best-chosen word. Thus, we have rephrased the introduction to reflect that, while the majority of the existing evidence supports the association between obesity and worse clinical response in PsA patients, contributing to this body of evidence with a new cohort of relatively big sample size is of interest. Additionally, we removed the mention to the Iannone et al. study in the introduction, and kept it only in the discussion of the manuscript.

- Introduction section:

“However, Iannone et al. found no statistically significant differences in remission rates among obese and normal weight PsA patients treated with TNFis (Iannone F. et al. 2013) 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.

- Page 5, lines 85-92:

“Despite the growing evidence on the association between obesity and worse clinical response in PsA patients, most published observational cohort studies on this topic had relatively small sample size. For example, a systematic review investigating the association between obesity and response in immune-mediated inflammatory diseases identified one randomised clinical trial and eight observational cohort studies in PsA patients, but six of the included observational cohorts had a sample size ≤330 (Singh et al. 2018). Thus, further investigating this effect, especially in a different and bigger population cohort, remains of interest. Additionally, it is unclear whether the findings would remain consistent across outcome definitions.”

➢ Reviewer 1, comment #5

Given such a wide observation window in your country's registry, why have you only considered the outcomes of your study at 12 months? What do we know about the information at 2 or 3 years?

Answer:

We appreciate this comment from the reviewer. While we agree that looking at longer time-frames would be of interest, this would be out of the scope of this paper, which addresses the early response or early clinical success after start of the patient’s first b/tsDMARD. If we would look further in time, the interpretation of the findings would need to address both early and secondary non-response, potentially in a different manner each. Thus, that would have been a completely different study design. Alternatively, with regard to the follow-up time, we did consider a shorter follow-up of 6-months. However, this was not feasible due to the very reduced number of visits during that short study period.

We appreciate reviewer’s point and hope that our explanation is sufficient to support our decision on follow-up.

Reviewer 1, comment #6

The cutaneous criterion within the MDA response is explicit (PASI or BSA) not just the clinician's opinion on this disease domain.

Answer:

Thank you for this point. We used the Minimal Disease Activity (MDA) outcome as available in the SCQM dataset. This variable was calculated by the data provider (SCQM) and we described it in the methods. Following the comment from the reviewer, we understand the need to highlight this in the limitations section of the manuscript. Thus, we have noted this accordingly.

▪ Page 16, lines 330-333:

“Additionally, while standard MDA definition includes Psoriasis Activity and Severity Index (PASI) ≤1 or body surface area (BSA) ≤3 (Coates et al. 2010), due to data restrictions our MDA definition included a skin manifestation of “none” or “almost none”, as reported by the physician.”

➢ Reviewer 1, comment #7

Although your study refers to biological or ts-DMARDS, the numbers you provide are, by far, referred to TNFi. I think you should comment on this in your methods and/or discussion. This becomes

relevant since the negative effect of obesity on TNFi persistence does not seem to be as important when other therapeutic routes are analysed, such as IL-17A inhibitors (Expert Opin Biol Ther. 2021 Dec;21(12):1539-1541) Answer:

We appreciate this comment from the reviewer and we agree that we should highlight in the manuscript the high percentage of patients with TNF inhibitors versus other b/tsDMARDs. Therefore, we have added this information to the discussion, in the strength and limitations section.

- Page 17, lines 354-356:

"It was suggested that obese patients may benefit from other non-TNFi b/tsDMARDs, however, the evidence is limited (Queiro 2021). Nevertheless, our results of a lower odds of achieving remission may be largely driven by the high TNFi use in our cohort."

Reviewer 1, comment #8

Your explanation as to why there is a disconnect between outcomes in terms of MDA or DAPSA remission and persistence of treatment is not very convincing. In fact, most clinicians are not usually inclined to prolong therapies in obese PsA patients who do not achieve treatment goals, but rather to seek alternative therapeutic routes to that of TNFi. In general, a non-response in the first 3-4 months of treatment usually leads to a change of treatment in routine clinical practice.

Answer:

Thank you for commenting on this. We understand that an explanation to the inconsistence between the clinical outcomes and the treatment persistence in our study can not be fully provided, since the study protocol does not provide the means for it. Thus, we tried to provide a hypothesis formulated based on our prior communications and discussions with rheumatologists in Switzerland.

However, we appreciate the comment from the reviewer, which contradicts our initial hypothesis. Thus, we have removed that statement from our discussion.

- Discussion section:

"Clinicians may be inclined to continue with therapy longer in obese than in normal weight patients, given the higher disease activity at baseline and knowing that obese patients may be less likely to achieve MDA or remission. While this could impact the time to treatment stop, it may not affect the persistence at a relatively advanced time-point."

➢ Reviewer 1, comment #9

Finally, as you rightly point out, the concept of remission is an evolving concept in the field of PsA, and more and more attention is being paid to the opinion of patients. In obese subjects, etiopathogenic aspects (already mentioned by you) surely coincide, along with others of a diverse nature, which ultimately have an influence on the way in which the patient experiences his/her disease, and which determine those remission rates that you observe, as well as the rate of therapeutic successes and failures. Perhaps you should reflect on this in your discussion.

Answer:

The reviewer raises a good point. We agree that the discussion of remission, particular in obese patients, is an ongoing discussion. Indeed, elements of pain and quality of life may have an influence on the perception of their disease. Additionally, treatment related aspects, including dosing and the inflammatory state of the patient. To better reflect this, we have added the following section to our discussion to address this topic.

- Page 15, lines311-318

"The reasons for the lower response rates in obese patients could be multiple. High body weight can affect the clearance and volume of distribution of b/tsDMARDs (Sharma et al. 2015; Fasanmade et al.

2009; Ternant et al. 2008). Adipose tissue has a proinflammatory capacity (Versini et al. 2014), which could negatively influence drug response. Finally, a relationship between mechanical stress and triggering of musculoskeletal inflammation (deep Köbner phenomenon) in psoriatic arthritis is discussed. Nevertheless, the observed lower odds of achieving MDA or remission in the obese group is of interest, and the consistency across the studied definitions of remission suggests that this effect may be reflected on several factors of the PsA disease."

Reviewer 2 Comments
Reviewer 2: Dr. B. Glintborg, Rigshosp
Competing interests of Reviewer: Research grants: pfizer, Biogen, AbbVie, Sandoz

➢ Reviewer 2, comment #1
This manuscript have several aims – mainly to explore b/tsDMARD treatment outcomes according to body mass index/obesity upon treatment start, but also to explore overlaps between a variety of treatment outcomes in PsA. The manuscript is based on data from the wellknown SCQM registry, but does not seem to have a rheumatologist in the author group. Although the manuscript is fairly well written, it also seems overly complicated and focusing on a clinical situation that is already well described. The only study that the authors bring forward illustrating conflicting previous results regarding the negative impact of obesity is 2013 (ref 17) including only 135 patients and likely having low power.
First and foremost, I suggest the authors to reconsider the presentation of knowledge gap and to rephrase accordingly.
Answer:
We would like to thank the reviewer for the very detailed review of our manuscript. We appreciate the constructive feedback provided by the reviewer, which it aids improving our manuscript.
We appreciate this comment from the reviewer and would like to address the several points mentioned.
First, regarding not having a rheumatologist as co-author, we would like to mention that we work hand-by-hand with several rheumatologists on a regular basis. We are pharmacoepidemiologists and healthcare professionals and we have already performed other studies on this topic and this data source. Thus, we had prior related discussions with rheumatologists. However, at the time of submitting this manuscript, none of our collaborators had contributed to this specific study to the point of fulfilling the authorship criteria. However, following the concerns from the reviewer, and since we agree with the benefits of multidisciplinary teams, we have included one of our collaborating rheumatologists with expertise in PsA as co-author (Dr. Raphael Micheroli). Dr. Micheroli has previously provided clinical expertise and has now contributed substantially to the revision of the manuscript during the response to peer-review. Additionally, we also continue to include Dr. Axel Finckh in our acknowledgement section based on the numerous discussions in other projects that inherently improved our understanding of the SCQM database.
Regarding the description of the knowledge-gap, we appreciate the comment from the reviewer and agree that this can be improved. Thus, we have re-phrased the introduction and we hope that the changes will be satisfactory. Additionally, we removed the mention to the Iannone et al. study in the introduction, and kept it only in the discussion.

- ✦ Authorship:

Enriqueta Vallejo-Yagüe[1], Theresa Burkard[1], Raphael Micheroli[2], Andrea M. Burden[1]
draft manuscript, and T.B., R.M., and A.M.B. contributed with revision and editing. All authors read and agreed to the published version of the manuscript.” ▪ Introduction section:

1 Department of Chemistry and Applied Biosciences, Institute of Pharmaceutical Sciences, ETH Zurich, Zurich, Switzerland.

2 Department of Rheumatology, University Hospital of Zurich, University of Zurich, Zurich, Switzerland.

- ✦ *Page 17, lines 370-373:*

“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

“However, Iannone et al. found no statistically significant differences in remission rates among obese and normal weight PsA patients treated with TNFis (Iannone F. et al. 2013) 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.

✦ Page 5, lines 84-91:

“Despite the growing evidence on the association between obesity and worse clinical response in PsA patients, most published observational cohort studies on this topic had relatively small sample size. For example, a systematic review investigating the association between obesity and response in immune-mediated inflammatory diseases identified one randomised clinical trial and eight observational cohort studies in PsA patients, but six of the included observational cohorts had a sample size ≤330 (Singh et al. 2018). Thus, further investigating this effect, especially in a different and bigger population cohort, remains of interest. Additionally, it is unclear whether the findings would remain consistent across outcome definitions.”

➢ Reviewer 2, comment #2

I have a line of additional comments:

It seems an important result is that obesity and overweight was frequent in the studied population. Could that be a result to be reported more clearly?

Answer:

The reviewer highlights an interesting point. We published last year a descriptive study on psoriatic arthritis (PsA) and rheumatoid arthritis (RA) patients from the SCQM registry, in which we compared the frequency of overweight and obesity in PsA and RA patients compared to the general population in Switzerland (Vallejo-Yagüe et al. 2021. doi.org/10.3390/jcm10143194). While we did not address this point in the current manuscript to avoid repetition, following the comment from the reviewer, we have now addressed it in the discussion.

▪ Page 15, lines 319-322:

“Finally, as described elsewhere (Vallejo-Yagüe et al. 2021), the prevalence of overweight and obesity were higher among PsA patients in comparison to the general population in Switzerland (Switzerland 2017, people >15 years old, 31% overweight and 11% obese) (https://www.bfs.admin.ch/asset/de/14147705). Higher obesity prevalence among PsA patients in comparison to the reference population was in agreement with prior studies (Vallejo-Yagüe et al. 2021).”

, comment #3

The authors wonder if patients with underweight should not have been included in the normal weight group. Could a sensitivity analyses excluding these patients be performed?

Answer:

We appreciate this comment and we agree with the reviewer’s interest on a sensitivity analysis. Thus, we have performed sensitivity analyses excluding the 12 underweight patients (BMI<18.5 kg/m^2) from the normal weight group. Overall, these sensitivity analyses show similar results than the study main findings.

▪ Page 9, lines 189-190:

“Another sensitivity analysis addressed the one-year outcomes after excluding patients with underweight (BMI<18.5 kg/m^2).” ▪ Page 12, lines 243-244:

“The sensitivity analysis excluding the 12 patients with BMI<18.5 yielded similar results to the main study findings (Supplementary Table S4).” ▪ Supplementary table:

Supplementary Table S4. Sensitivity analyses, excluding the 12 patients with body mass index (BMI) <18.5 kg/m^2. Result from the multivariable logistic regression investigating the association between body mass index (BMI) categories and various clinical outcomes, with maximum followup 12-months.

Sensitivity analyses		Maximum follow-up 12-months

(Excluding BMI<18.5)	n sample size	n vents	OR	ORadj		
MDA						
Normal weight	294	62 (21.1)	1 (ref.)	1 (ref.)		
Overweight	285	40 (14.0)	0.61 (0.39-0.95)	0.65 (0.40-1.06)		
Obese	183	19 (10.4)				
DAPSA-remission			0.44 (0.25-0.77)	0.45 (0.24-0.84)		
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)				
DAPSA-remLDA			0.38 (0.20-0.75)	0.43 (0.21-0.88)		
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)				
cDAPSA-remission			0.68 (0.44-1.06)	0.70 (0.42-1.14)		
Normal weight	294	294 (18)	1 (ref.)	1 (ref.)		
Overweight	285	39 (13.7)	0.72 (0.46-1.14)		0.81 (0.49-1.33)	
Obese	183	16 (8.7)	0.45 (0.25-0.81)		0.53 (0.28-1.00)	
DAS28-remission						
Normal weight	294	110 (37.4)				
Overweight	285	109 (38.2)	1.00 (0.71-1.42)		0.89 (0.61-1.31)	
Obese	183	51 (27.9)				
Treatment persistence at the end of follow-up	294	179 (60.9)	0.65 (0.44-0.98)	0.51 (0.32-0.82)		
Normal weight			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; DAPSAremission 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.

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, comment #4

Title:

Suggest to more clearly state that patients starting first b/tsDMARD were included Answer:

Thank you for this comment. We agree that it would be of interest to add to the title that the study is on new-users of b/tsDMARDs. However, since using acronyms in titles is not recommended, adding 'new-users of biologic or targeted synthetic disease modifying anti-rheumatic drugs' to the title would result in an excessive length. Following the editor's comments, we have now modified the title to: "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." We leave the decision on including in the title 'new-users of b/tsDMARD' to the editor.

➢ Reviewer 2, comment #5

Abstract:

The conclusion should include all aims put forward, also the overlapping of study outcomes.

Answer:

Thank you for this good reminder. We have added a statement on the overlapping of study outcomes to the conclusions in the abstract.

▪ Page 2, lines 54-55:

"High overlapping of patients achieving the outcomes MDA and cDAPSA-remission was observed across every BMI group."

➢ Reviewer 2, comment #6

I wonder why the authors use the phrase 'accordance' – without explaining the difference between accordance and overlap?

Answer:

We had overlooked the potential for confusion, as 'accordance' and 'overlap' are synonyms of agreement. However, we understand that there could be slight differences between both words, and we therefore appreciate the comment from the reviewer. Following this point, we have revisited the use of both words in our manuscript. We therefore concluded that using only the term overlapping may be clearer (and more descriptive) for the reader. We hope that the reviewer agrees with this decision.

We have removed the term 'accordance' from everywhere in the text where it could be substituted by 'overlapping' or where both terms were mentioned (e.g., "Additionally, accordance or overlapping across study outcomes was investigated.")

, comment #7

Strengths and limitations:

The authors state that the source used was optimal – without explaining why. However, only half of patients had complete data and imputation was needed. Suggest to phrase in a more objective manner.

Answer:

We assume that the reviewer refers to the table placed after the abstract, named "Strengths and limitations of this study". We consider the data optimal because it includes clinical endpoints (e.g.,

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tender and swollen joint counts, composite disease activity scores), which enable more suitable outcome definitions to assess clinical success in comparison to the often-used treatment persistence (in other observational studies). Additionally, this registry includes information on body mass index (BMI), a variable very often lacking in real-world-data (RWD). Finally, regarding the missingness, there is no nationwide RWD without missingness, thus, we do not consider this a specific limitation of our study, but an intrinsic limitation of observational research in RWD. Following the reviewers comment we have re-phrased the statement in the strengths and limitation table, and revisit the strengths and limitations subsection of the Discussion:

▪ Page 3, journal table titled "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." ▪ Page 16, lines 324-326:

In addition to the large sample size and availability of BMI information (often lacking in real-worlddata), the key strength of this study is the use of several relevant clinical outcome definitions.

▪ Page 16, lines 334-335:

Intrinsic to real-world-data, missingness was a limitation. We addressed missingness at baseline with multiple imputation and missingness during follow-up with sensitivity analyses.

, comment #8

The current strengths and limitations appear unstructured – with a mixture of statements, limitations and study descriptions. Suggest to rephrase in a more stringent and structured (and briefer?) manner

Answer:

Similar to the above, we assume that the reviewer refers to the table placed after the abstract, named "Strengths and limitations of this study". After the reviewer's comment we have re-visited and re-phrased the statements in this section.

▪ Page 3, journal table titled "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.

Reviewer 2

- 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."

➢ Reviewer 2, comment #9

Methods:

This whole study is based on a single measurement of weight and height. Did the authors consider the validity of these measurements – e.g. were they measured or selfreported by the patients themselves?

Answer:

This information is measured and entered by the rheumatologist during routine clinical visits, and is therefore not self-reported. Using more than one measurement was not considered optimal due to the time range between recorded weight and height information. However, we trust that this information was recorded appropriately.

Reviewer 2

, comment #10

Main outcome was MDA within first year. What was the time-window for evaluating this outcome – and how was early withdrawal handled?

Answer:

MDA was assessed within the first year after the index-date. Since the index-date was the date when the patient started their first b/tsDMARDs, we assessed MDA within the 365.42 days after that. Thus, the time-window for collecting this outcome, or in other words, the follow-up time, was from day 1 to 365 after the index date. Thus, the outcome information was collected during the whole year after the start of the patient's first b/tsDMARD, and any record of achievement of MDA during follow-up classified the patient as MDA-achiever.

Since the follow-up time was one year for every patient and this study is performed in registry data, we did not need to handle 'withdrawal' as such. However, in this scenario, right attrition occurs when a patient does not have any record or information on the outcome during the follow-up time.

In this case, for our main analysis, these patients were classified as not achievers of the outcome. However, we tested this assumption in the sensitivity analyses excluding these patients.

- Page 6, lines 119-120:

"The primary outcome was defined as achievement of MDA within the first year after the index date."

- Page 6, line 125:

"Secondary outcomes assessed within the first year were: […]" ▪ Page 7, lines 134-135:

"As a tertiary outcome, persistence with the first b/tsDMARD at the end of month-12 was assessed."

- Page 7, lines 137-139:

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

, comment #11

The authors put forward a line of co-variates. But I miss a definition of these – e.g. how was low education defined? What inflammatory markers were included (CRP?), was the joint count based on 28 or 66 joints? How was comorbidities evaluated – selfreported by patient, in patient files? According to mediciation use? The authors put forward the term 'fragility', how was this evaluated?

Answer:

Due to the high number of covariates, we did opt to truncate out explanation in the text. However, we appreciate that this can lead to some ambiguity. To address the specific questions put forth by the reviewer, we provide more details below:

- High education was defined as 'höhere Fachschule (university of applied sciences), Universitätsstudium (university study) ', and the no category for this variable was defined by 'obligatorische Schule (compulsory school)' or 'Berufslehre (apprenticeship), Maturitätsschule (3-4 year high school that enables direct admission to Universities school)'. Together with the SCQM team we tried to translate these terms into English and it is complicated since the education system in Switzerland is unique compared to other regions (e.g., North America or the UK). Thus, we decided to keep it simple and only mention 'high education', which includes university education.
- The fragility or health standardized surveys were the Health Assessment Questionnaire [HAQ] and the Short Form-12 [SF-12]. We included the term 'fragility' to distinguish these surveys from simply comorbidity indexes. However, following the comment from the reviewer, we opted for referring to them only as health standardized surveys and not measurements of fragility.
- To our knowledge, comorbidity information is collected by both physician and patient, but it is mainly a patient-reported outcome.

We modified the comorbidities subsection as follows:

Reviewer 2

▪ Pages 7-8, lines 149-163:

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

, comment #12

Data analyses:

The DAG diagram seems interesting, why was comorbidities (in text and figure) and education (in text) not mentioned/included?

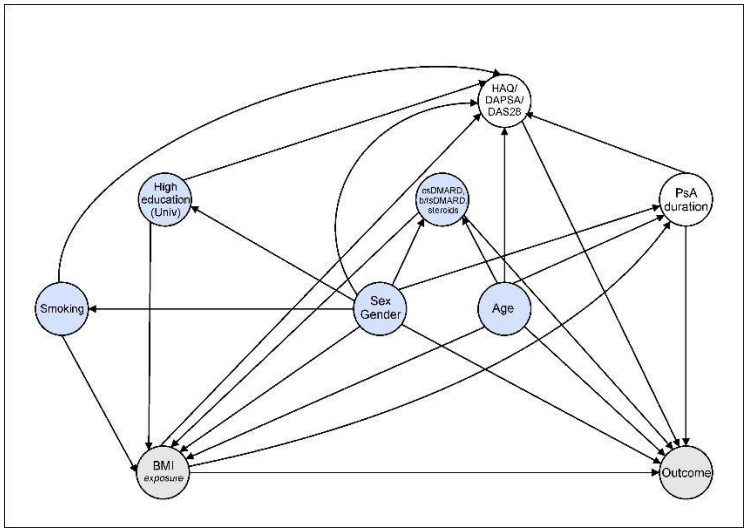
Answer:

Thank you for this comment. We have adapted the text in the methods section, the Supplementary Figure S4 and its legend.

- Pages 8-9, lines 182-188:

“Confounders were chosen based on clinical rational and direct acyclic graphs (DAGs) (Supplementary Figure S4), and included: sex (male; female), age, high education (yes/no), ever smoking (yes/no), b/tsDMARD (TNFi; other biologic; tsDMARD), csDMARD at index date (yes/no), and corticosteroid use at index date (yes/no). Additionally, sensitivity analyses were performed whereby we added the respective composite disease activity score or health standardized survey to the fully adjusted models for primary and secondary outcomes to assess their potential mediating impact on the analyses.”

- Supplementary Figure S4 and its legend:



“Supplementary Figure S4. Direct acyclic graph (DAG) displaying the clinical rational for selection of confounders. The nodes represent the exposure, outcome and covariates, and the lines or edges represent the assumed relationship between them. Grey nodes represent the exposure and the

- **Reviewer 2**

outcome. Blue nodes represent the confounders included in the study full adjusted model. White nodes represent other variables included in sensitivity analyses."

, comment #13
It seems as if treatment retention during one year of follow-up was evaluated as a yes-no outcome instead of a traditional time to event analysis which could be better use of the data available and which also could include censoring/lack of followup in a meaningful way. What was the reason for this decision?
Answer:
Thank you for this important comment. While we agree on the benefits of survival analyses when investigating treatment survival, that was not the goal of this study. Instead, treatment persistence (not survival) was a tertiary outcome in our study, selected to complement the primary and secondary outcomes (MDA or remission within the first year). The purpose of assessing treatment persistence at 12-months was to study whether continuing on treatment for one year would reflect the same findings as the study clinical outcomes.

- Reviewer 2, comment #14

Patient and public involvement
It is unfortunate that patients were not involved – or a rheumatologist? Please comment?
Answer:
Regarding involvement of rheumatologists please see our answer to your comment #1.
On regard to patient involvement, there are patients with immune-mediated diseases with whom we consult general enquires. However, they are not PsA patients and we did not include them in a formal manner, thus, we do not consider that we can claim that there was patient involvement in the manuscript. We will keep this in mind for future manuscripts and work with our collaborating rheumatologists to identify potential patient organizations.

- Reviewer 2, comment #15

Table 1:
Please indicate what comparison p-value refers to – especially the p-value in the right column (compared to normal weight?) Answer:
Thank you for this comment. We have included this information both in the methods section and in the Table 1 footnote.
▪ Page 8, lines 165-169:
"Patient baseline characteristics were described, and the overweight and obese categories were compared to the normal weight group (reference group) using chi-squared test for categorical variables and t-test, ANOVA, or Kruskal-Wallis test for continuous variables. For these tests, missing values did not function as a grouping variable. Statistical significance was defined as $p \leq 0.05$." ▪ Table 1 footnote:
"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."

Reviewer 2

, comment #16

What is the scale for global skin manifestation?

Answer:

The reviewer brings up a very good point. In SCQM, the physician global skin manifestation is a categorical variable including the below-described categories. The physician decides on the category according to their own medical judgement. Thus, a more detailed description of this scale is out of our knowledge.

none < almost none < mild < mild to moderate < moderate < moderate to severe < severe

➢ Reviewer 2, comment #17

Figure 1, Supplementary Table S2, S3

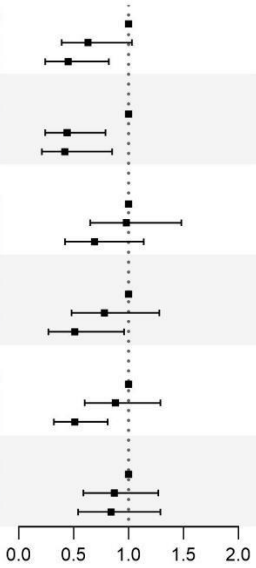
The authors use the terminology 'n events', does this refer to patients achieving the outcome? Suggest to show not only events but also total number in group?

Answer:

Thank you for this suggestion. We agree that adding total numbers along with the number of outcomes (n events) would benefit the tables and figures. Thus, we did so in Figure 1, Table 2, and Supplementary Table S2, S3, and the new S4. Additionally, we took the chance to also add the corresponding percentage of patients achieving each outcome within each BMI group. Thus, the former Supplementary Table S4 is no longer needed and was therefore removed.

- Figure 1:

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



OR: odds ratio adjusting for: sex, age;

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

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

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

comment #18

Supplementary Figure S2

Please describe meaning of the colors shown and the scale used in the right side of Figure Answer:

Thank you for this comment. We have added this info in the legend.

- Supplementary Figure S2 legend:

"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."

- Reviewer 2, comment #19

Supplementary Figure S4
There seem to be blue, grey and white nodes, and there to be filled and dotted lines. Please explain all details.
Answer:
Please see the answer to the comment #12.

- Reviewer 2, comment #20

Supplementary Figure S5
The interesting patient group excluded are those that were eligible for inclusion (PsA, b/tsDMARD treatment, age >18 and correct time period) BUT did not have data on weight and height. Suggest to restructure the figure accordingly.
Answer:
We understand the point highlighted by the reviewer. While we foresee the benefit of adapting the table as suggested, this flow diagram corresponds to the specific steps performed during the coding process. Thus, we rather keep them as they are now. Thank you for your understanding.

VERSION 2 – REVIEW

REVIEWER	Queiro, Ruben Department of Rheumatology, HU, Central de Asturias
REVIEW RETURNED	14-Jun-2022

GENERAL COMMENTS	Dear Authors, Thank you for considering all my comments and suggestions. Your manuscript looks now improved. Congrats.

REVIEWER	Glintborg, B. Rigshosp
REVIEW RETURNED	28-Jun-2022

GENERAL COMMENTS	Thank you to the authors for adding changes to the manuscript according to suggestions which I think have improved the paper to a large extent. I have one major concern which is the definition and measurement of the MDA (and probably also other outcome measures). The authors explain that this occurred already from 1 day since treatment start. Clearly, outcomes measured so soon after treatment start does not make sense as the treatment would not have had impact so early during follow-up. What was the median time to outcome evaluation in the dataset? And the IQR? I guess this time window is similar for all outcome measures reported? If it turns out that many patients were evaluated very soon after baseline, this should be emphazised and discussed? Otherwise I only have minor details to add:

Reviewer 2

	The validity of registry-based research largely/solely rely on the data given and how these are interpreted. Thus, I suggest for transparency to add all explanations of covariates to the manuscript (e.g. educational level, comorbidities, skin manifestations). This could be in a footnote or supplementary as preferred. The fact that measures of height and weight are measured in the clinic is a huge benefit (as compared to self-reported), and I suggest this added to main text, method section. #20: I am not convinced that Suppl Figure S5 should be according to coding procedures? – and still suggest it to reflect stepwise patient-selection as suggested. Strengths and limitations: the phrasing 'leading to a wide picture' seems vague, suggest to rephrase in a more stringent manner in accordance to aims The last sentence: 'with respective involvement' could be rephrased to ' with this phenotype' ?

VERSION 2 – AUTHOR RESPONSE

Reviewer 1 – Comments II

Reviewer 1: Dr. Ruben Queiro, Department of Rheumatology, HU, Central de Asturias

➢ Comments to the Author:

Dear Authors,

Thank you for considering all my comments and suggestions. Your manuscript looks now improved. Congrats.

Answer:

Thank you.

Reviewer 1 – Comments II

Reviewer 2: Dr. B. Glintborg, Rigshosp

Comments to the Author:

Thank you to the authors for adding changes to the manuscript according to suggestions which I think have improved the paper to a large extent.

➢ Reviewer 2, comment #1

I have one major concern which is the definition and measurement of the MDA (and probably also other outcome measures). The authors explain that this occurred already from 1 day since treatment start. Clearly, outcomes measured so soon after treatment start does not make sense as the treatment would not have had impact so early during follow-up. What was the median time to outcome evaluation in the dataset? And the IQR? I guess this time window is similar for all outcome measures reported? If it turns out that many patients were evaluated very soon after baseline, this should be emphazised and discussed?

Answer:

Reviewer 2

Thank you for the interesting comment. Following the request from the reviewer, we provided here a table with the median and interquartile range (IQR) of the time from index date to the follow-up record used to assess MDA, DAPSA-remission, and DAS28-remission, all within the one-year follow-up after the index date (Table R1). Additionally, we depicted here the cumulative density distribution for the time to the record used to assess MDA, DAPSA-remission, and DAS28-remission, stratified by BMI group (Figure R1, below). Finally, we added a comment on this topic in the Discussion section.

- Page 16, lines 337-341

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

Table R1. Median days and interquartile range [IQR] from index date to the follow-up record used to assess MDA, DAPSA-remission, and DAS28-remission. Only patients with record of the outcome during follow up are included.

	Time (days) to MDA record Median [IQR]	Time (days) to DAPSA record Median [IQR]	Time (days) to DAS28 record Median [IQR]
Normal weight	214 [104-324]	245 [112-335]	196 [94-330]
Overweight	245 [110-323]	290 [121-337]	253 [122-326]
Obese	226 [108-328]	226 [112-325]	213 [105-319]

Abbreviations: MDA Minimal Disease Activity; DAPSA Disease Activity for Psoriatic Arthritis; DAS28 Disease Activity Score 28-joints; IQR Interquartile range.

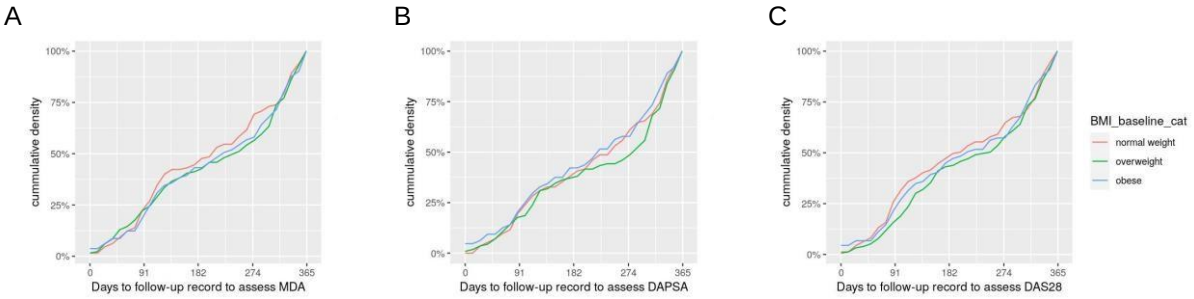


Figure R1. Cumulative density of the days from index date to the follow-up record used to assess MDA (A), DAPSA-remission (B), and DAS28-remission (C). Only patients with outcome information during follow-up (first 12-months after index date) were included.

➢ Reviewer 2, comment #2

Otherwise I only have minor details to add: The validity of registry-based research largely/solely rely on the data given and how these are interpreted. Thus, I suggest for transparency to add all explanations of covariates to the manuscript (e.g. educational level, comorbidities, skin manifestations). This could be in a footnote or supplementary as preferred.

Answer:

Reviewer 2

We understand that information on codes for medication or diseases could have been expected (e.g., ATC codes, or MedDRA codes). However, the SCQM does not use drug or disease dictionaries, and information is collected as specific variables of the SCQM database. Following the comment from the reviewer, we added additional information on covariates in the supplementary material. We also added to the Table 1 footnote the list of b/tsDMARDs included as TNF inhibitors, other biologics, and tsDMARD.

- Page 8, line 166

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

- Supplementary Text S1. Additional information on covariates.

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

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

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

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

- Table 1

	Normal weight (n=306)	Overweight (n=285)	p-value	Obese (n=183)	p-value
[…]	[…]	[…]	[…]	[…]	[…]
b/tsDMRAD			0.87		0.35
TNFi biologic[a]	279 (91.18)	262 (91.93)		160 (87.43)	
other biologic[b]	9 (2.94)	9 (3.16)		6 (3.28)	
tsDMARD[c]	18 (5.88)	14 (4.91)		17 (9.29)	
[…]	[…]	[…]	[…]		
[…]				[…]	[…]

[…]

Reviewer 2

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

- Reviewer 2, comment #3

The fact that measures of height and weight are measured in the clinic is a huge benefit (as compared to self-reported), and I suggest this added to main text, method section.

Answer:

Thank you. We have followed this recommendation and we added this information in the Methods section.

- Page 6, lines 116-117

  “Measures of height and weight are taken in the clinic, during routine visits to the rheumatologist.”

- Reviewer 2, comment #4

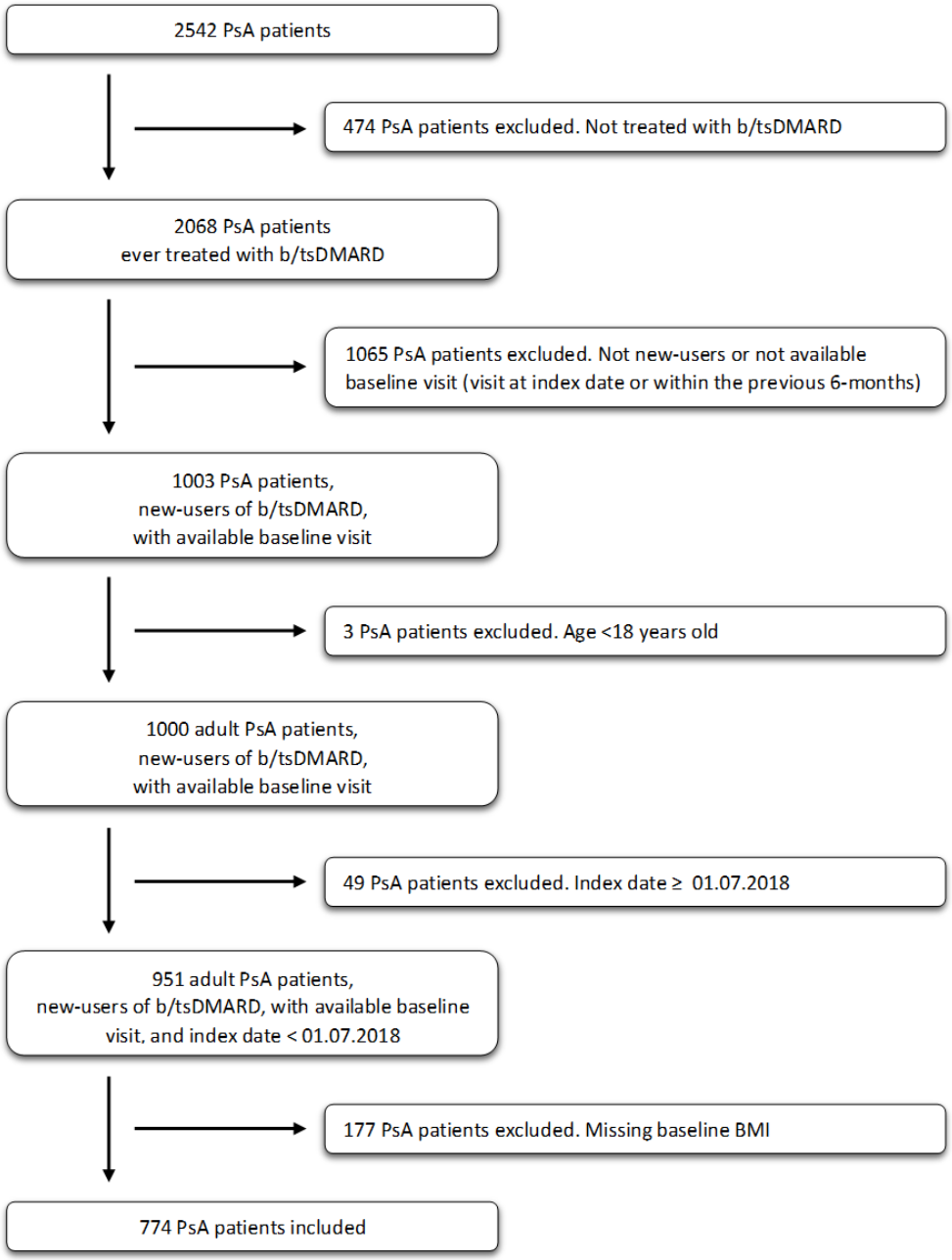
#20: I am not convinced that Suppl Figure S5 should be according to coding procedures? – and still suggest it to reflect stepwise patient-selection as suggested.

Answer:

Following the suggestion, we have modified the figure, showing the exclusion due to lack of baseline BMI as last step.

- Supplementary Figure S5.

Reviewer 2



- Reviewer 2, comment #5

Strengths and limitations: the phrasing ‘leading to a wide picture’ seems vague, suggest to rephrase in a more stringent manner in accordance to aims. The last sentence: ‘with respective involvement’ could be rephrased to ‘with this phenotype’?

Answer:

Following the reviewer’s comment, we rephrased the suggested text in the ‘Strengths and limitations of this study’ section to the following:

Reviewer 2

Strengths and limitations of this study

[…]

► 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.

[…]

► 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.

VERSION 3 – REVIEW

REVIEWER	Glintborg, B. Rigshosp
REVIEW RETURNED	24-Aug-2022

GENERAL COMMENTS	Thank you to the authors for addressing the comments forwarded by the reviewers. I have no further comments