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ORIGINAL RESEARCH

Importance of quick attainment of minimal disease activity for a positive impact on lives of patients with psoriatic arthritis

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ABSTRACT

Objective To compare patient-reported outcomes (PROs) from the first year to the third year between patients with psoriatic arthritis (PsA) who achieved minimal disease activity (MDA) in the first year after diagnosis and those who did not.

Methods Consecutive, newly diagnosed, patients with DMARD naïve PsA with oligoarthritis or polyarthritis were selected from the Dutch southwest Early PsA cohoRt. Patients were categorised in three groups: (1) Patients who were in MDA at both 9 months and 12 months after diagnosis (sustained MDA); (2) Patients who achieved MDA in the first year but in whom it was not sustained at both 9 months and 12 months (non-sustained MDA); (3) Patients who did not achieve MDA in the first year (no MDA). PROs were compared between groups from the first year to the third year after diagnosis using a linear mixed model.

Results 240 patients were selected; 104 (43%) were classified as sustained MDA, 60 (25%) as non-sustained MDA and 76 (32%) as no MDA. Patients who did not achieve MDA in the first year experienced remarkably lower PROs during follow-up, compared with the sustained MDA group: health status (European Quality of life 5-Dimensions 5-Levels) was 0.23 units lower (95% CI −0.28 to −0.18), functional impairment (Health Assessment Questionnaire-Disability Index) was 0.81 units higher (95% CI 0.70 to 0.92), pain (Visual Analogue Scale) was 35.38 mm higher (95% CI 30.57 to 40.18), fatigue (Bristol Rheumatoid Arthritis Fatigue-Multidimensional Questionnaire) was 17.88 units higher (95% CI 14.60 to 21.16), and anxiety and depression (Hospital Anxiety and Depression Scale) were, respectively, 3.26 units (95% CI 2.25 to 4.27) and 4.04 units higher (95% CI 3.10 to 4.99).

Conclusion Failure to achieve MDA in the first year after PsA diagnosis was associated with worse PROs that persisted over the years.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Patients with psoriatic arthritis who achieve minimal disease activity (MDA) have better health-related quality of life (HRQoL) and mental well-being, and are less fatigued than patients who do not reach MDA.

WHAT THIS STUDY ADDS

⇒ This is the first study exploring the impact of achieving MDA in the first year after PsA diagnosis and the long-term effects on patient-reported outcomes (PROs).

⇒ Failure to achieve MDA in the first year after diagnosis was associated with remarkably poorer HRQoL and health status, more functional limitations, fatigue and pain, and higher anxiety and depression scores over the course of 3 years, compared with patients who did achieve sustained MDA in the first year.

⇒ Differences in PROs between patients who did and did not achieve (sustained) MDA were large and persisted during follow-up despite intensified treatment with biologic DMARDs, emphasising the importance of achieving early MDA in patients with PsA.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our study shows that early achievement of MDA in PsA is important for long-term benefits.

INTRODUCTION

Psoriatic arthritis (PsA) is a heterogeneous disease with multifaceted clinical manifestations.[1] Clinical manifestations include arthritis, sacroiliitis, enthesitis, dactylitis and psoriasis, but also uveitis and inflammatory bowel disease. These symptoms lead to a high burden of disease.[2]

Treatment is aimed at symptom reduction and prevention of structural damage. Over the last decades, new therapeutic options have led to substantially improved clinical outcomes.[3] Moreover, healthcare is increasingly shifting towards a patient-centred care approach. In

patient-centred care not only clinical outcomes, but also patient-reported outcomes (PROs) play an important role, with a focus on the individual patient experience, preferences and healthcare needs.[4] However, the heterogeneous nature of PsA has led to much discussion about the most appropriate treatment target. The PsA community supports the use of minimal disease activity (MDA), a composite measure that includes most of the clinical manifestations and PROs.[5] It is increasingly accepted as a clinically important outcome.[6 7] MDA can be used as a treatment goal in a treat-to-target (T2T) approach or to compare treatment efficacy.[8 9]

Previous studies have shown that patients with PsA who achieve MDA are less fatigued and have better health-related quality of life (HRQoL), mental well-being and worker productivity than patients who do not reach MDA.[10 11] The importance of achieving MDA within the first year for improved HRQoL at 12 months has also been demonstrated.[11] However, there are hardly any studies with long-term data to support this. One study showed that sustained MDA, defined as MDA at ≥3–4 consecutive visits, was associated with fewer functional limitations and better general health over a 5-year period.[12] However, data on achieving (sustained) MDA early and the resulting long-term effect on PROs are lacking. Moreover, there is—to our knowledge—no study that includes almost all of the International Consortium for Health Outcome Measurement (ICHOM) domains.[13]

Therefore, the aim of this study is to investigate whether PROs, measuring most of the ICHOM domains, differ over the course of 1–3 years after diagnosis between patients with PsA who achieved sustained MDA within the first year, patients who achieved MDA within the first year but in whom it was not sustained, and patients who did not achieve MDA within the first year after diagnosis.

METHODS

Patients

Data from the Dutch southwest Early Psoriatic Arthritis cohoRt (DEPAR) were used, which is a multicentre, prospective real-world cohort study. Patients with newly diagnosed DMARD naïve PsA are eligible for inclusion. Inclusion started in August 2013 and is ongoing. Written informed consent was obtained from all participants according to the Declaration of Helsinki. Further details on the DEPAR Study have been described elsewhere.[14]

For this study we selected all consecutive patients with PsA, categorised as oligoarthritis (2–5 joints) or polyarthritis (>5 joints) at baseline by their treating rheumatologist, who were included between 2013 and 2018. These patients with PsA (n=337) (online supplemental figure S1) were subdivided into three groups based on their MDA status during the first year of follow-up. Patients were considered in MDA when they achieved at least five of the following seven criteria: tender joint count (TJC 68) ≤1, swollen joint count (SJC 66) ≤1, body surface area (BSA) ≤3%, pain (Visual Analogue Scale (VAS)) ≤15 mm, patient global disease activity (VAS) ≤20 mm, Health Assessment Questionnaire (HAQ) ≤0.5 and Leeds Enthesitis Index (LEI) ≤1.[5] Patients were categorised in three groups by achievement of MDA in the first year: (1) 'sustained MDA' that includes patients who were in MDA at both their 9-month and 12-month visits, (2) 'non-sustained MDA' that includes patients who achieved MDA in the first year but in whom it was not sustained at both their 9-month and 12-month visits, and (3) 'no MDA' that includes patients who did not achieve MDA in the first year.

Data collection

In the first year patients were evaluated every 3 months, half-yearly in the second year and subsequently once a year. At each visit data were collected on clinical outcomes, DMARD usage and PROs.

Clinical outcomes included SJC, TJC, enthesitis (LEI) and psoriasis (BSA).[15 16] Medication data included all prescribed medication for PsA, which are extracted from the electronic health records. Treatment decisions were made based on the insight of the treating rheumatologist and in shared decision with the patient.

Patients filled out online questionnaires at each visit, including the following PROs: pain, global disease activity, functional ability, health status, HRQoL, fatigue and emotional health impact. Pain and global disease activity were measured on a 0–100 mm VAS, where higher scores indicate poorer health status.[17] The HAQ-Disability Index (HAQ-DI) was used to measure functional ability.[18] The HAQ-DI consists of eight domains and patients indicate the degree to which they experienced difficulties in the past week with daily activities. The total score ranges from 0 to 3 and higher scores represent more functional impairment. Health status was measured with the European Quality of life 5-Dimensions 5-Levels (EQ-5D-5L) Questionnaire.[19] The EQ-5D-5L measures five health dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression). This yields a health state that is converted into a health utility index score, reflecting a health status as compared with the general population of the Netherlands.[20] Scores range from 0 to 1; 0 equals death and 1 equals perfect health. The 36-item Short Form Health Survey (SF-36) was used to capture HRQoL.[21] It measures eight domains; physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional and mental health. Each domain is scored on a 0–100 scale and higher scores indicate a better HRQoL. Physical Component Summary (PCS) and Mental Component Summary (MCS) Scores are calculated from these domains.[22] Fatigue was measured with the Bristol Rheumatoid Arthritis Fatigue-Multidimensional Questionnaire (BRAF-MDQ).[23] Scores range from 0 to 70 and higher scores indicate greater severity of fatigue. Emotional health impact was measured with the Hospital Anxiety and Depression Scale (HADS).[24] The HADS consists of an anxiety and depression subscale, with scores ranging

from 0 to 21 per subscale. A score >7 is suggestive of the presence of an anxiety disorder or depression.[25]

Statistical analysis

To examine possible differences in patient characteristics between MDA groups at baseline, an analysis of variance, Kruskal-Wallis test or χ^2 test was used, when appropriate. Furthermore, a linear mixed model (LMM) with an unstructured covariance matrix and covariates MDA group, time (months since baseline), sex, age and SJC was used to compare PROs over the course of 1 year to 3 years after diagnosis between groups. The minimal clinically important difference (MCID) per PRO was compared with the estimated mean difference between groups.[26–31]

If five MDA criteria were met and two were missing, MDA was considered achieved since missing information could not alter MDA status. Likewise, if three MDA criteria were not met, MDA was considered not achieved, regardless of missing data for the remaining four criteria. If MDA status could be changed by missing information, MDA status was found missing. If MDA status was missing at one visit, and MDA status before and after that visit was both in MDA or both not in MDA, we set the MDA status at the missing visit equal to that state. If at baseline MDA was missing and the patient was not in MDA at all other visits during the first year, then baseline visit was set at no MDA.

We hypothesised that PRO data were not missing at random. Therefore, multilevel joint modelling with multiple imputations (n=20, jomo), was performed.[32] Imputation models for the EQ-5D-5L, SF-36, BRAF-MDQ and HADS included sex, age, TJC and SJC as independent variables. The HAQ-DI and VAS pain were not imputed, because these PROs are two of the criteria that form MDA.

Since MDA state was not ascertained for all patients due to missing data, baseline characteristics of patients with an MDA group (n=240) were compared with those who were not assigned to an MDA group (n=97) (online supplemental table S1). Furthermore, we performed a sensitivity analysis using complete cases in our LMM (online supplemental table S2) and provided crude estimates of the PROs after 2 years and 3 years to ensure validity of our results (online supplemental table S3).

To correct for multiple testing, we applied a Bonferroni correction to the LMMs by multiplying calculated p values with the 19 performed tests. A corrected value of $p \leq 0.05$ was considered statistically significant. Analyses were performed in Stata V.17.0 and R V.4.1.2.

RESULTS

We included 337 patients with PsA with oligoarthritis or polyarthritis who had their baseline visit before March 2018, of whom 240 (71%) could be categorised into an MDA category. Of these, 104 (43%) were classified as sustained MDA, 60 (25%) as non-sustained MDA and 76 (32%) as no MDA. At baseline, patients had a mean (SD) age of 52.8 (14) years, 122 were male (51%) and median (IQR) symptom duration was 9.4 (4–31) months (table 1).

Table 1 Baseline characteristics of study patients

	Sustained MDA **(n=104)**	Non-sustained MDA **(n=60)**	No MDA **(n=76)**	**P value**
Demographic characteristics				
Age (years), mean±SD	51.9±13	52.5±14	54.3±13	0.510
Sex (male), n (%)	64 (62)	27 (45)	31 (41)	**0.013**
Symptom duration (months), median (IQR)	7.6 (4–24)	7.8 (4–29)	12.3 (5–46)	0.107
Disease activity				
Swollen joint count (66), median (IQR)	3 (2–6)	3 (1–5)	4 (2–8)	0.136
Tender joint count (68), median (IQR)	3 (1–6)	3 (2–8)	7 (3–13)	**<0.001**
Psoriasis, n (%)	85 (84)	54 (91)	66 (85)	
BSA in case of psoriasis, median (IQR)	2.5 (1.5–4)	2.5 (1–6.5)	4 (2–7)	0.085
Enthesitis, n (%)	27 (26)	28 (44)	38 (58)	
LEI in case of enthesitis, median (IQR)	1 (1–2)	2 (1–2)	2 (1–4)	**0.016**
HAQ, median (IQR)	0.38 (0.13–0.75)	0.63 (0.50–0.88)	1.0 (0.63–1.38)	**<0.001**
Global (VAS), median (IQR)	30 (14–56)	45 (26–65)	58 (42–74)	**<0.001**
Pain (VAS), median (IQR)	26 (11–51)	47 (25–66)	65 (50–80)	**<0.001**
CRP (mg/L), median (IQR)	6 (2–13)	4 (0–12)	5 (1–10)	0.246

A value of p<0.05 was considered statistically significant and is shown in bold.
BSA, Body Surface Area; CRP, C reactive protein; HAQ, Health Assessment Questionnaire; LEI, Leeds Enthesitis Index; MDA, Minimal Disease Activity; VAS, Visual Analogue Scale.

Table 2 Estimated mean differences in patient-reported outcomes during follow-up (1–3 years) for MDA groups

	Sustained MDA (n=104)	Non-sustained MDA (n=60)		No MDA (n=76)	
		β (95% CI)	Bonferroni corrected *P* value*	β (95% CI)	Bonferroni corrected *P* value*
Pain (VAS)	Ref	15.80 (10.71 to 20.89)	**<0.001**	35.38 (30.57 to 40.18)	**<0.001**
Fatigue (BRAF-MDQ)	Ref	7.87 (4.40 to 11.33)	**<0.001**	17.88 (14.60 to 21.16)	**<0.001**
Functional ability (HAQ-DI)	Ref	0.31 (0.19 to 0.43)	**<0.001**	0.81 (0.70 to 0.92)	**<0.001**
Health status (EQ-5D-5L)	Ref	−0.07 (−0.12 to −0.03)	**0.048**	−0.23 (−0.28 to −0.18)	**<0.001**
PCS (SF-36)	Ref	−6.77 (−8.77 to −4.78)	**<0.001**	−13.51 (−15.41 to 11.62)	**<0.001**
MCS (SF-36)	Ref	−3.07 (−5.64 to −0.50)	0.37	−7.51 (−9.95 to −5.08)	**<0.001**
Anxiety (HADS)	Ref	1.34 (0.26 to 2.42)	0.28	3.26 (2.25 to 4.27)	**<0.001**
Depression (HADS)	Ref	1.30 (0.30 to 2.30)	0.21	4.04 (3.10 to 4.99)	**<0.001**

β shows the estimated mean difference comparing the sustained MDA group with the other two groups over the course of 1–3 years of follow-up.
All analyses were adjusted for age, sex and swollen joint count.
A value of p<0.05 was considered statistically significant and is shown in bold.
*n=19.
BRAF-MDQ, Bristol Rheumatoid Arthritis Fatigue-Multidimensional Questionnaire; EQ-5D-5L, European Quality of life 5-Dimensions 5-Levels; HADS, Hospital Anxiety and Depression Scale; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCS, Mental Component Summary; MDA, Minimal Disease Activity; PCS, Physical Component Summary; SF-36, 36-item Short Form Health Survey; VAS, Visual Analogue Scale.

Patients in the no MDA group were more often female than in the sustained MDA group, and they had higher TJC, LEI, HAQ and VAS scores at diagnosis than patients in both the sustained and non-sustained MDA groups (table 1). Patients with non-sustained MDA were also more often female and had significantly higher baseline HAQ and VAS scores than patients with sustained MDA.

Pain

Pain over the course of 1–3 years of follow-up was on average 35.38 mm (VAS) higher for the no MDA (95% CI 30.57 to 40.18) and 15.80 mm higher for the non-sustained MDA (95% CI 10.71 to 20.89) groups compared with the sustained MDA group (table 2, figure 1A). Estimated mean differences between groups exceeded the MCID (≥10 mm).[26]

Fatigue

Similarly, patients in the no MDA and non-sustained MDA groups experienced more severe fatigue during follow-up; 17.88 units (95% CI 14.60 to 21.16) and 7.87 units (95% CI 4.40 to 11.33) higher, respectively, than those in sustained MDA (table 2, figure 1B). Estimated mean differences between groups exceeded the MCID (≥7.4).[27]

Activity limitation

Functional impairment, assessed with the HAQ-DI, was more severe from the first year to the third year of follow-up in the non-sustained MDA group; mean scores were 0.31 units higher (95% CI 0.19 to 0.43) compared with patients in sustained MDA. Likewise, the no MDA group experienced more activity limitation than patients in sustained MDA; they scored 0.81 units higher (95% CI 0.70 to 0.92) on the HAQ-DI (table 2, figure 1C). For the latter comparison the estimated mean difference exceeded the MCID (≥0.35).[31]

Emotional and physical well-being

Both general (EQ-5D-5L) and more specific (SF-36, HADS) questionnaires were used to measure health status and HRQoL.

Patients with sustained MDA had the highest health status (EQ-5D-5L) over time, followed by non-sustained MDA and no MDA (table 2, figure 1D). Estimated mean differences between MDA groups exceeded the MCID (≥0.07).[28] A similar trend was seen for anxiety and depression scores (HADS), although the MCID (≥1.7) was not exceeded for the comparison between non-sustained and sustained MDA (table 2, figure 1E,F).[30]

The SF-36 PCS and MCS were lower in patients not in MDA compared with patients with non-sustained or sustained MDA. In addition, the PCS was lower in patients with non-sustained MDA compared with those with sustained MDA (table 2). For the SF-36 PCS the MCID (≥2.5–5) was exceeded between all MDA groups.[29] For the SF-36 MCS estimated mean differences were only larger than the MCID (≥2.5–5) for no MDA versus sustained MDA.[29] After 2 years, SF-36 domain scores of sustained MDA patients were comparable to the general Dutch population, while patients with non-sustained MDA and no MDA had lower scores (figure 2A).[33] After 3 years, the non-sustained MDA group had improved to similar values as the general population on the mental components of the SF-36, but scored lower on general

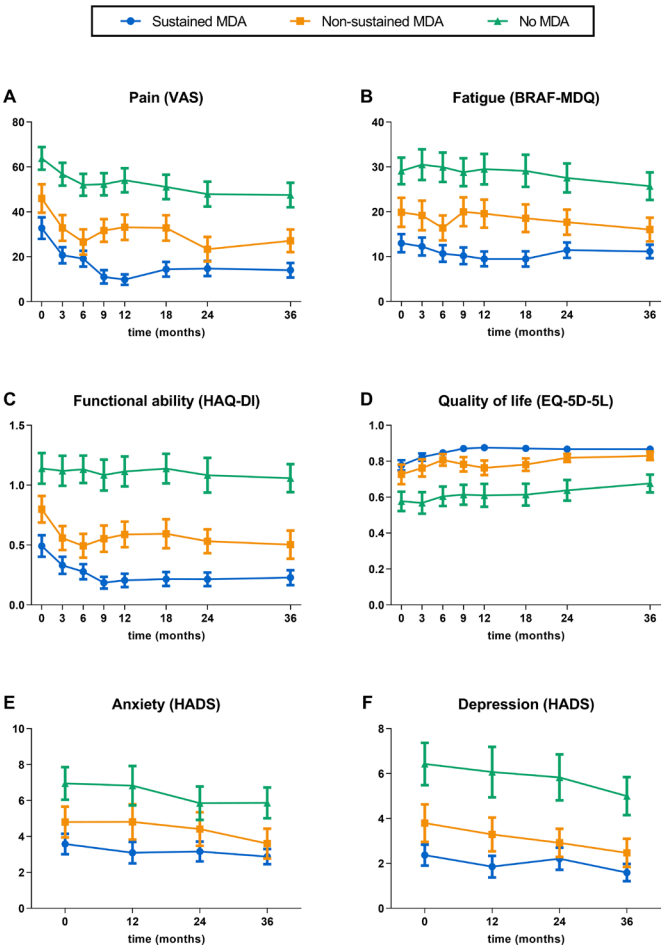

Figure 1 Patient-reported outcomes over 3 years of follow-up. Values are the mean (95% CI). BRAF-MDQ: Bristol Rheumatoid Arthritis Fatigue-Multidimensional Questionnaire; EQ-5D-5L: European Quality of life 5-Dimensions 5-Levels; HADS: Hospital Anxiety and Depression Scale; HAQ-DI: Health Assessment Questionnaire–Disability Index; MDA, Minimal Disease Activity; VAS: Visual Analogue Scale.

health perceptions and the physical components. Patients not in MDA still reported low scores on all SF-36 domains (figure 2B).

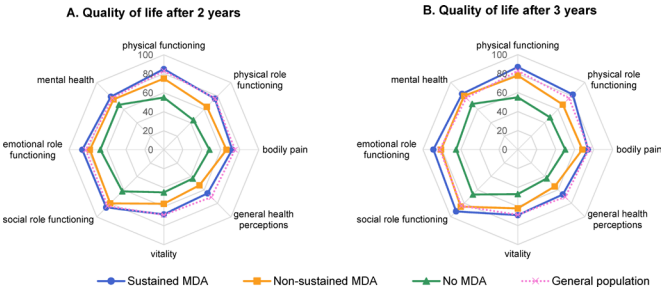

Figure 2 Health-related quality of life for minimal disease activity (MDA) groups and the general Dutch population. (A) Mean health-related quality of life scores after 2 years. (B) Mean health-related quality of life scores after 3 years. Health-related quality of life was measured with the short form-36 domains. Health-related quality of life for MDA groups was compared with the general Dutch population norms (adapted from Aaronson *et al* [33]).

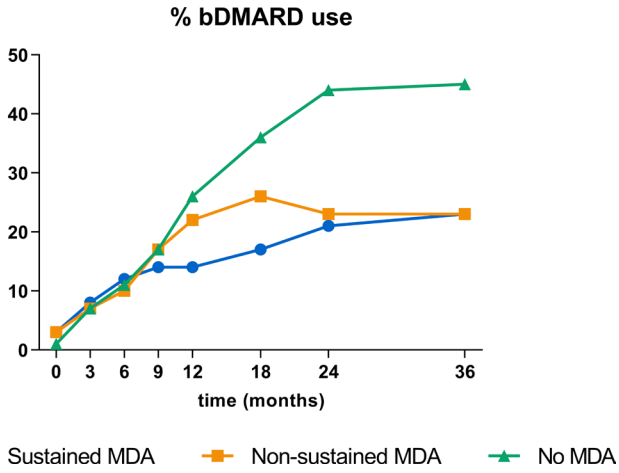

Figure 3 Biologic DMARDs usage for minimal disease activity groups. The percentage of patients per minimal disease activity (MDA) group who uses a biologic DMARD over time.

Thus, emotional and physical well-being remained remarkably worse in the no MDA group compared with the sustained MDA group over the course of 3 years.

DMARD-therapy

Treatment alterations occurred in all MDA groups, but most treatment intensifications were done in the no MDA group which is best reflected by the biologic DMARD (bDMARD) prescriptions (figure 3). After 3 years bDMARD usage was 23%, 23% and 45%, respectively, in the sustained MDA, non-sustained MDA and no MDA group.

Sensitivity analyses

In the sensitivity analyses, baseline characteristics of patients in an assigned MDA group were compared with those who could not be categorised in an MDA group due to missing data. Baseline characteristics were similar except for age, HAQ and VAS global and pain scores (online supplemental table S1). We also compared PROs over time of our imputed data set with the complete cases and found similar results (online supplemental table S2). Crude estimates of PROs after 2 years and 3 years without adjustments for confounders (sex, age, SJC) are available in online supplemental table S3.

DISCUSSION

Patients who failed to achieve MDA in the first year after PsA diagnosis, had a significantly higher disease burden over the two following years than those who achieved sustained MDA, with regards to pain, fatigue, functional impairment, HRQoL, health status and anxiety and depression. The differences between the two groups were large, especially for the HAQ-DI, where the no MDA group scored more than four times higher than the sustained MDA group. For the former group, HAQ-DI scores after 3 years were similar to their scores at the time of diagnosis, despite ongoing treatment. Estimated

mean differences between groups exceeded MCIDs for all aforementioned PRO measures, emphasising the relevance of the observed effect. Patients with non-sustained MDA experienced more severe pain, fatigue, functional impairment and a lower physical HRQoL compared with patients in sustained MDA. In contrast, HRQoL of patients who reached sustained MDA in the first year was comparable to the general Dutch population during follow-up. Aforementioned differences in PROs persisted despite intensified treatment.

Our results show an association between achieving MDA and better PRO scores in patients with PsA. Although some studies have investigated this relationship before, this is the first study demonstrating the importance of achieving MDA in the first year after diagnosis.[8 10–12] To our knowledge, only one study investigated intervening early and aiming for tight disease control in a T2T approach in PsA. The TICOPA Study, with MDA as treatment target, showed that patients who achieved MDA had significantly better clinical outcomes for both joints and skin after 48 weeks.[8] In rheumatoid arthritis (RA) the added value of achieving early and sustained remission with a T2T approach and its positive effect on health outcomes has already been widely proven.[34]

There are several possibilities to explain the observed differences between the MDA groups. In our study, patients who did not achieve MDA in the first year were more often women and seemed to have a longer symptom duration, which was consistent with findings from previous studies.[35 36] Early initiation of treatment leads to better long-term health outcomes in patients with PsA.[36] In addition, an early start of bDMARDs results in a higher proportion of patients achieving MDA.[37] Since a diagnostic delay is still common in PsA and methotrexate monotherapy is the first treatment step according to GRAPPA and EULAR guidelines, earlier and more aggressive treatment could potentially lead to better outcomes.[3 38 39] Patients not in MDA also had a higher disease activity at baseline, both on subjective (VAS scores, HAQ, TJC) and objective disease activity measures (SJC, enthesitis). In addition to active inflammation, other mechanisms are likely to account for the inability to achieve MDA. To gain more insight into the cause of these differences, we compared residual disease activity between groups. Residual disease activity was more frequently present in the no MDA group and mostly caused by both high VAS scores (pain and global) and HAQ after 3 years. Nevertheless, patients not in MDA also scored worse on objective measures, that is, higher SJC and LEI than the other MDA groups (39% SJC >1 in the no MDA group vs 17% in the other groups) (online supplemental table S4). This indicates that in the no MDA group, inflammation continues to play a role despite intensified treatment. Even after adjusting for SJC the differences in PROs between MDA groups persisted. Another reason for residual disease activity might be the high prevalence of depression and anxiety in PsA, respectively, 37% and 22%. Mental health problems have an effect on quality of life and pain scores.[40] For example, SF-36 MCS scores are affected by depression/anxiety and anxiety is also correlated with physical well-being.[41 42] In addition, we know that in RA symptoms of depression and anxiety are associated with reduced treatment response.[43] We cannot be sure that other comorbidities (such as central pain sensitisation or fibromyalgia) differ between MDA groups. These comorbidities might in themselves lead to worse PROs and might, therefore, influence the relationship between achieving MDA and long-term PROs.

Nevertheless, the difference in PRO scores over the course of 1–3 years of follow-up in patients who achieve MDA in the first year and those who do not is large. Since PsA is a heterogeneous disease, it is important to treat all its facets. Earlier and more aggressive treatment with, for example, bDMARDs might be one of the solutions, since methotrexate, the most commonly used drug in PsA, primarily works in arthritis and psoriasis.[39] In addition, comorbidities such as mental health problems should be recognised early and attended to as needed. First and foremost, we probably need to look beyond medication and, therefore, a holistic approach is essential to reduce the impact of the disease.

One strength of this study is that DEPAR includes patients with PsA who receive usual care. Therefore, outcomes of this study are more generalisable than those from trials, as there is less risk of selection bias. On the other hand, due to the observational nature of our study, treatment varies widely, which could cause confounding, especially in the relationship between achieving MDA and PROs on the long-term. To account for confounding, we adjusted all analyses for SJC, as this is associated with treatment choice. Another strength of our study is that clinical data collection is performed by research nurses in a standardised manner, which ensures reliable data collection. However, this may have led to differences between treatment strategy and disease activity, since the former is determined by the rheumatologist's insight and his own assessment of disease activity and is thus independent of the nurses' assessment. Patients with PsA in DEPAR have relatively low disease activity. Extrapolating our results to a PsA population with a higher disease activity would mainly affect the 'no MDA' group and their PROs would be worse. Differences between the sustained MDA and no MDA groups would then become even larger. Therefore, we believe that our results are generalisable to other PsA populations with higher disease activity levels.

A limitation of our study is that many PROs across different ICHOM domains are measured, which has led to multiple testing. To account for multiple testing we applied a Bonferroni correction and compared estimated mean differences to published MCIDs from literature.[26–31] Moreover, we found consistent PRO domain differences between MDA groups, without contradictory results. Our results are also comparable to previous literature. For example, we have previously shown that achievement of MDA is associated with better functional ability

and quality of life, and other studies have found similar results.[11 44] In our study, there might be selective dropout (online supplemental figure S1). Patients with sustained MDA might drop out because of inactive disease, while patients not in MDA might drop out due to dissatisfaction with their treatment. These differences may have led to an underestimation of our results, in which case the true differences in PRO scores between MDA groups may be even larger. Furthermore, some patients were not categorised into an MDA group due to missing data. Therefore, we compared baseline characteristics of these patients with those who were assigned an MDA group (online supplemental table S1). Baseline characteristics were similar, except for younger age and higher HAQ and VAS pain and global scores in patients not categorised in an MDA group. This shows that our results are valid despite missing data.

In conclusion, patients who did not reach a state of MDA in the first year after diagnosis had a substantial disease burden that persisted over the years despite intensified treatment with bDMARDs. In patients who did achieve sustained MDA, PROs were comparable to the general Dutch population after 2 years and 3 years of follow-up. To reduce the burden of PsA, early intensive treatment focusing on all facets of the disease, including associated comorbidities, is necessary. In patients who do not achieve MDA despite early escalation of therapy, we need to look beyond bDMARDs and be aware of comorbidities and other factors that affect their ability to achieve MDA.

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Collaborators On behalf of Cicero.

Contributors SVJSH performed the statistical analysis and drafted the manuscript. PHPdJ, MV and JL contributed to the analysis. All authors contributed to the design, revised the manuscript, and read and approved the final manuscript. MV is the guarantor.

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Competing interests SW and ARP are UCB stockholders.

Patient consent for publication Not applicable.

Ethics approval This study was approved by the medical ethics committee of Erasmus Medical Center Rotterdam, the Netherlands (MEC-2012-549). Participants gave written informed consent to participate in the study before taking part.

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