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EXTENDED REPORT

Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis

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ABSTRACT

Objectives (1) To investigate the demographic and clinical characteristics contributing to the delay from symptom onset to the first visit to a rheumatologist; (2) to compare clinical, radiographic and patient-reported outcome measures of those who saw a rheumatologist early in their disease course with those who were diagnosed later.

Methods All psoriatic arthritis (PsA) patients, fulfilling CASPAR criteria, with an average disease duration of >10 years were invited for detailed clinical evaluation. The total lag time from symptom onset to their first rheumatological encounter was studied. The data were extracted from the referral letters and medical records. Patients were classified as early consulters or late consulters depending on whether they were seen by a rheumatologist within or beyond 6 months of symptom onset.

Results 283 PsA patients were studied. Median lag time from the disease onset to the first rheumatological assessment of the cohort was 1.00 years (IQR 0.5–2). 30% (n=86), 53% (n=149) and 71% (n=202) of the cohort were seen by a rheumatologist within 6 months, 1 and 2 years of symptom onset, respectively. PsA patients with low education status (OR 2.09, p=0.02) and Body Mass Index (OR 0.92, p=0.01) were significantly more likely to have a diagnostic delay of >2 years. On multiple stepwise regression analysis, the model predicted significant association of late consulters with the development of peripheral joint erosions (OR 4.25, p=0.001) and worse Health Assessment Questionnaire scores (OR 2.2, p=0.004).

Conclusions Even a 6-month delay from symptom onset to the first visit with a rheumatologist contributes to the development of peripheral joint erosions and worse long-term physical function.

INTRODUCTION

Psoriatic arthritis (PsA) is a progressive inflammatory musculoskeletal disease which if untreated leads to joint damage and disability. PsA was formerly considered a milder form of arthritis but an inception cohort study has shown that 47% of the PsA patients who presented within 5 months of onset of symptoms had ≥1 erosion by the second year of follow-up despite the fact that the majority had been treated with disease-modifying antirheumatic drugs (DMARDs).[1] In another study, 67% of PsA patients demonstrated ≥1 radiographic erosion at their initial presentation to a rheumatologist.[2] Given the propensity for the early occurrence of destructive disease, prompt diagnosis of PsA is the first step towards optimal patient management. Despite the increasing primary care physician and dermatologist awareness of PsA, the prevalence of undiagnosed PsA remain high. A recent study of psoriasis patients attending a dermatology clinic has shown that 29% of patients had undiagnosed PsA.[3] Delay in diagnosis in turn delays introduction of appropriate disease-modifying treatment and may contribute to poor patient outcome.

In rheumatoid arthritis (RA), the importance of rapid assessment by a rheumatologist is now well established,[4 5] where the delay from symptom onset to the first visit with a rheumatologist or start of therapy has been reported to range from several months to more than 1 year.[6–9] The data from early arthritis clinics show that rheumatological assessment in <12 weeks is associated with less joint destruction and a higher chance of achieving DMARD-free remission as compared with a longer delay in assessment.[9] In RA, a UK study has shown that increasing the proportion of patients treated with DMARDs within 3 months of symptom onset, from a currently estimated figure of 10% to a figure of 20%, could result in productivity gains for the economy of £31 million over 5 years.[10]

In a PsA cohort study, 65% of patients were diagnosed in less than 1 year from the symptom onset.[11] In another study, clinical and radiographic damage was more marked in patients presenting with >2 years of disease duration.[12] Similarly, delayed PsA diagnosis has been shown to be associated with worse physical function.[11] Antirheumatic treatment should ideally be started within a few months after the onset of symptoms, and the delay in assessment by rheumatologists of patients with PsA is potentially an important determinant of delay in treatment initiation. To date, no study has addressed the clinical characteristics or outcomes of those patients in whom there is a lengthy lag time from symptom onset to the first rheumatological encounter.

In a large, cross-sectional cohort of PsA patients, the objectives of this study were: (1) to investigate the demographic and clinical characteristics associated with the delay from symptom onset to the first visit with a rheumatologist; (2) to compare clinical, radiographic and patient-reported outcome measures (PROMs) in those who saw a rheumatologist early in the disease course with those who were seen later.

METHODS

All patients attending rheumatology clinics at St Vincent's University Hospital, Dublin, with a confirmed diagnosis of PsA, as per the internationally

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agreed CASPAR criteria (Criteria of the ClASsification of Psoriatic ARthritis), were suitable for inclusion. Among them, a cohort of patients with an average disease duration of >10 years were identified, and then invited for detailed cross-sectional evaluation.

The total lag time from PsA-related symptom onset to the first rheumatological encounter (also referred in the text as diagnostic delay) was recorded. The data were extracted from the referral letters and medical records in order to determine the time of disease onset, defined as onset of stiffness, pain or joint swelling, and the following first visit to a rheumatologist. Patients were classified as early consulters or late consulters depending on whether they were seen by a rheumatologist within or beyond 6 months of symptom onset. Additionally, we broke down the cohort further into those seen within 1 year or within 2 years from the onset of their PsA-related symptoms.

Following informed consent, patients underwent a detailed skin and rheumatological assessment including disease activity measures. For skin psoriasis (PsO), the extent and severity of skin psoriasis was assessed by the Psoriasis Area and Severity Index (PASI), which is the most widely used tool for the measurement of severity of psoriasis. Moreover, we also measured body surface area (BSA) to estimate the extent of skin disease. For PsA, physical examination included recording the number of tender and swollen joints using the 68 tender/66 swollen joint counts, the presence of dactylitis, the presence of enthesitis, as well as the number of permanently deformed joints. Clinically deformed joints were defined as the presence of fixed deformities, flail joints, fused joints and surgically replaced joints.[13] We also recorded prior usage of DMARDs and whether the psoriatic disease (PsO and/or PsA) required tumour necrosis factor inhibitor (TNFi) therapy. The inflammatory markers (erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)) were measured at the time of assessment and in addition, through medical record review, we documented the maximum levels of CRP and ESR ever achieved during a flare of inflammatory arthritis. Maximum ever PASI, BSA, tender joint counts and swollen joint counts were also extracted through extensive medical record view.

A number of different PROMs were recorded, for example, Health Assessment Questionnaire (HAQ), Dermatology Life Quality Index, Bristol Rheumatoid Arthritis Fatigue Numeric Rating Scale and short form-36 (SF-36). SF-36 V.2 was used and individual physical and mental component summary scores (PCS.SF-36 and MCS.SF-36) were recorded. Radiographs were taken of involved joints along with hands, feet and sacroiliac joints of all these patients (n=283).

The clinical variables studied were gender, smoking habits, Body Mass Index (BMI), units of alcohol intake per week, family history of PsO and PsA, different clinical types of PsO, psoriatic nail disease, duration of PsO and PsA, PsO and PsA age of onset, and educational attainment of the cohort. Education status was stratified by whether participants completed secondary (high) school education. This study was approved by the local Medical Research Ethics committee. This study was carried out in the Republic of Ireland, where general practitioners (GPs) are the first point of contact for patients with any acute or chronic illness. GPs are usually able to diagnose and manage a significant majority of these medical problems; however, in some cases, an expert opinion is required and the GP will refer the patient usually by letter to a hospital consultant. The patient then will be prioritised by the consultant team and an outpatient appointment will be arranged where following assessment and investigations, treatment can be initiated.

Statistical analysis was performed using the SPSS software, V.17. Significance was defined as $p<0.05$ (two-tailed). A χ^2 statistic was used to investigate the distributions of categorical variables, and continuous variables were analysed using Student t test. We applied ORs and associated CIs to measure association between different variables. The association of clinical variables with different lag times were determined using univariate and multivariate logistic regressions. The factors associated with late consultations on univariate analysis with significance at the 0.25 level were entered into a multivariable model. The model was then reduced by backward elimination until the remaining effects were significant at the 0.05 level. Estimates of regression coefficients were obtained from this final model.

RESULTS

A total of 283 PsA patients (mean age 54.6±12 years; 52% women; mean PsA duration of 19±9 years; 25% with sacroiliitis; 44.5% with radiographic peripheral joint erosions; 8% with arthritis mutilans; 60% of patients requiring TNFi for PsA, mean maximum PASI of 5.7±5.2, mean current PASI 2.1) were studied. There were no missing data on any of these patients (n=283) as all patients were assessed in a dedicated research clinic where all the above mentioned clinical, laboratory and radiographic details were collected.

Median lag time from the disease onset to the first rheumatological assessment of the cohort was 1.00 years (IQR 0.5–2). Overall, 30% (n=86) of the cohort was seen by a rheumatologist within 6 months of symptom onset. Similarly, 53% (n=149) and 71% (n=202) of the cohort were reviewed within 1 and 2 years of the disease onset, respectively. Table 1 compares the demographic and clinical characteristics of patients who were seen within 6 months, 1 and 2 years with those who were seen later in the disease course. Regarding the clinical characteristics contributing to diagnostic delay, we found a significant association of low BMI, along with a borderline association of low education status with the delay of >2 years from symptom onset to the first visit to a rheumatologist.

After a long-term follow-up of this cohort of 283 patients (mean PsA duration of 19 years), on univariate analysis we found that late consulters (>6 months delay at first rheumatologist encounter) had significantly more erosions (OR 4.58, $p \leq 0.001$), osteolysis (OR 3.6, p=0.01), sacroiliitis (OR 2.28, p=0.01), arthritis mutilans (OR 10.6, p=0.02), deformed joints (OR 2.28, p=0.002), number of deformed joints (OR 1.06, p=0.006), more DMARDs/TNFi failures (OR 1.47, p=0.007), less patients achieving drug-free remission (OR 0.42, p=0.01) and worse functional disability as reflected by the HAQ scores (OR 2.17, p=0.003). However, on multiple stepwise regression analysis (table 2), the model predicted significant association of late consulters with the development of peripheral joint erosions (OR 4.25, p=0.001) and worse HAQ scores (OR 2.2, p=0.004).

Table 3 shows univariate and multivariate associations of demographic, clinical associations and adverse outcomes of delayed diagnosis of >1 year. We found that on multiple stepwise regression analysis, delayed diagnosis of more than 1 year is significantly associated with the development of arthritis mutilans (OR 2.66, p=0.050), lower chances of achieving drug-free remission (OR 0.44, p=0.04), worse physical component of quality of life (OR 1.05, p=0.001) and worse functional disability as reflected by HAQ scores (OR 2.11, p=0.008). Similarly, on multiple stepwise regression analysis, a delayed diagnosis of more than 2 years is associated with low education status (OR 2.09, p=0.02), low BMI (OR 0.92, p=0.01), peripheral joint

Table 1 Baseline demographics and patient characteristics associated with different time lags from symptom onset to the first rheumatological encounter

	Delayed diagnosis of >6 months			Delayed diagnosis of >1 year			Delayed diagnosis of >2 years		
	No (n=86)	Yes (n=197)	p Value	No (n=149)	Yes (n=134)	p Value	No (n=202)	Yes (n=81)	p Value
Age (years±SD)	53±11	55±12	0.32	53.8±12	55.4±11	0.25	54±12	56±12	0.20
Gender—% Male	46.5	48	0.85	48	46	0.73	47.8	46	0.81
Smoking—%	41	45	0.48	41.9	45	0.58	43.8	43.8	0.98
BMI (score±SD)	29±6	29±5	0.77	29±5.5	28.9±5	0.46	29.7±5.6	27.4±4.6	0.001
Low education status—%	15	23	0.13	16	25	0.054	17.7	27.5	0.060
PsO age of onset (years±SD)	27±13	28±15	0.74	27.6±14	27.4±14	0.88	27.5±14	27.7±14	0.85
PsA age of onset (years±SD)	36±13	34±12	0.45	35±13	34.5±12	0.57	35±13	34±12	0.51
Time from PsO to PsA development—(years±SD)	8±11	7±10	0.28	7.4±10	7±11	0.39	7.7±10	6.2±12	0.28
PsA duration (years±SD)	17±9	20±9	0.008	18±9	20.8±9	0.015	18±9	21.7±8.9	0.009
Family history of PsO—%	67	61	0.29	63	62.8	0.94	61.6	66	0.46
Family history of PsA—%	16	17	0.84	17	17	0.93	19	11	0.10
Oligoarthritis—%	12	5.5	0.07	9	5	0.18	8	5	0.31
Dactylitis—%	54	53	0.91	54	51	0.62	52	55	0.67
Deformed joints—%	51	71	0.002	61	69	0.18	60.6	75	0.022
Number of deformed joints (score±SD)	3.8±5.8	6.7±8.6	0.001	5±7	6.7±9	0.10	5±7	8±9	0.01
DMARDs free—%	21	10	0.01	18	8	0.01	16	7	0.060
Number of DMARDs failure—(score±SD)	0.98±0.78	1.3±1.0	0.002	1.2±0.98	1.2±1.0	0.91	1.2±0.98	1.2±1.0	0.91
Erosions—%	21	55	<0.001	39	51.4	0.03	39.9	56.3	0.01
Osteolysis—%	6	18	0.006	11	19	0.059	12.4	20.3	0.09
Sacroiliitis—%	15	29	0.01	20	30	0.059	22.7	30	0.19
Arthritis mutilans—%	1	11	0.005	4	13	0.008	5.9	13.8	0.030
PCS.SF-36—(score±SD)	43±11	43±10	0.63	41.8±11	44±9.9	0.056	42±11	46±10	0.006
MCS.SF-36—(score±SD)	45±12	47±11	0.22	45.8±12	48.4±10.6	0.06	46±12	48±11	0.21
HAQ—(score±SD)	0.43±0.48	0.66±0.58	0.001	0.55±0.56	0.64±0.57	0.16	0.55±0.55	0.70±0.59	0.04
BRAF—(score±SD)	14±4.5	15±5	0.18	14±4.9	14.5±5.4	0.42	14±5	14±6	0.79
DLQI—(score±SD)	2.5±4	2.6±3.8	0.81	2.4±3.8	2.7±4	0.40	2.4±3.7	3±4.6	0.30

BMI, Body Mass Index; BRAF, Bristol Rheumatoid Arthritis Fatigue Numeric Rating Scale; DLQI, Dermatology Life Quality Index; DMARDs, disease-modifying antirheumatic drugs; HAQ, Health Assessment Questionnaire; MCS.SF-36, mental health factors of quality of life; PCS.SF-36, physical health factors of quality of life; PsA, psoriatic arthritis; PsO, psoriatic disease.

erosions (OR 1.76, p=0.04), worse physical component of quality of life (OR 1.08, $p \leq 0.001$) and worse HAQ scores (OR 3.49, $p \leq 0.001$) (table 4).

DISCUSSION

There has been a growing interest in the early referral and early institution of therapy in PsA, with much of the initial data

Table 2 Univariate and multivariate regression models associated with the delayed rheumatological consultation of >6 months (adjusted simultaneously for variables shown)

	Univariate model			Multivariate model		
	OR	95% CI	p Value	OR	95% CI	p Value
Low education status	1.66	0.84 to 3.2	0.14			
Oligoarthritis	0.44	0.18 to 1.10	0.08			
PsA duration	1.04	1.01 to 1.07	0.009			
Deformed joints	2.28	1.35 to 3.85	0.002			
Number of deformed joints	1.06	1.01 to 1.10	0.006			
DMARDs/TNFi free	0.42	0.21 to 0.85	0.01			
No. of DMARDs/TNFi failures	1.47	1.11 to 1.95	0.007			
Erosions	4.58	2.5 to 8.2	<0.001	4.25	2.32 to 7.99	<0.001
Osteolysis	3.6	1.3 to 9.5	0.01			
Sacroiliitis	2.28	1.17 to 4.44	0.01			
Arthritis mutilans	10.6	1.4 to 80.6	0.02			
PCS.SF-36	0.99	0.97 to 1.02	0.73			
MCS.SF-36	1.01	0.99 to 1.03	0.15			
HAQ	2.17	1.30 to 3.61	0.003	2.20	1.29 to 3.74	0.004

DMARDs, disease-modifying antirheumatic drugs; HAQ, Health Assessment Questionnaire; MCS.SF-36, mental health factors of quality of life; PCS.SF-36, physical health factors of quality of life; PsA, psoriatic arthritis.

Table 3 Univariate and multivariate (adjusted simultaneously for variables shown) associations of different demographic details and clinical variables with the delayed diagnosis of >1 year

	Univariate model			Multivariate model		
	OR	95% CI	p Value	OR	95% CI	p Value
Low education status	1.77	0.98 to 3.1	0.056	1.72	0.93 to 3.18	0.08
PsA duration	1.03	1.00 to 1.06	0.01			
Deformed joints	1.39	0.85 to 2.28	0.18			
Number of deformed joints	1.02	0.99 to 1.05	0.10			
Erosions	1.61	1.00 to 2.59	0.04			
Osteolysis	1.90	0.96 to 3.75	0.06			
Sacroiliitis	1.68	0.97 to 2.91	0.06			
Arthritis mutilans	3.46	1.32 to 9.06	0.011	2.66	1.00 to 7.15	0.050
DMARDs/TNFi free	0.40	0.19 to 0.85	0.01	0.44	0.20 to 0.97	0.04
PCS.SF-36	1.02	0.99 to 1.04	0.057	1.05	1.02 to 1.08	0.001
MCS.SF-36	1.01	0.99 to 1.04	0.06			
HAQ	1.33	0.88 to 2.02	0.17	2.11	1.21 to 3.69	0.008

DMARDs, disease-modifying antirheumatic drugs; HAQ, Health Assessment Questionnaire; MCS.SF-36, mental health factors of quality of life; PCS.SF-36, physical health factors of quality of life; PsA, psoriatic arthritis.

extrapolated from the RA literature. There is a paucity of data regarding the time-dependent adverse outcomes related to delayed diagnosis in PsA. The concept of delay in receiving rheumatology care would only be important if it could be established that such a delay results in poorer function long-term or is associated with increased joint damage, and this study clearly shows that the diagnostic delay of even 6 months can lead to significantly more radiographic damage and worse physical function.

This is the first time that negative impact of various time delays to receiving rheumatology care has been simultaneously documented in an established cohort of PsA. To the best of our knowledge, there have been only two studies to date in PsA in which diagnostic delay has been examined. A UK study has shown that symptom duration of >1 year before the diagnosis is associated with worse physical function in PsA.[11] Similarly, another study has shown that clinical and radiological damage in PsA was higher among patients presenting later than 2 years of symptom onset.[12]

Our study provides an important extension to PsA literature regarding different time-dependent adverse outcomes related to delayed diagnosis. A number of novel observations were made. For example, first, as regards the clinical features influencing the delay in diagnosis, we studied the impact of low education status on delayed diagnosis, and used this as a surrogate for lower socioeconomic status. There are several measures of socioeconomic status, such as education,[14] income,[15] employment status and occupation.[16] One could speculate that low education level may be associated with worse outcomes in PsA. This study shows that PsA patients with low education status are significantly more likely to have a diagnostic delay of >2 years even after adjusting for confounders (OR 2.09, p=0.02), and that this diagnostic delay can lead to worse physical, functional and radiographic damage. Second, we have found a strong relationship between low BMI in PsA patients and delayed diagnosis of >2 years. Interestingly, recent studies in RA have shown that low BMI is adversely associated with radiographic joint damage and impaired quality of life.[17 18] The reason for the association between low BMI and diagnostic delay is unclear but one could speculate that patients with low BMI are less likely to receive medical attention compared with those who are overweight or obese.

Third, regarding the outcome of HAQ as a measure of physical disability in PsA, this was noted to have important

Table 4 Univariate and multivariate (adjusted simultaneously for variables shown) associations of different demographic details and clinical variables with the delayed diagnosis of >2 years

	Univariate model			Multivariate model		
	OR	95% CI	p Value	OR	95% CI	p Value
BMI	0.91	0.87 to 0.97	0.002	0.92	0.87 to 0.98	0.01
Low education status	1.76	0.95 to 3.2	0.069	2.09	1.07 to 4.07	0.02
Deformed joints	1.95	1.09 to 3.48	0.024			
Number of deformed joints	1.04	1.01 to 1.07	0.008			
Erosions	2.00	1.18 to 3.37	0.009	1.76	1.00 to 3.09	0.04
Osteolysis	1.79	0.90 to 3.58	0.09			
Sacroiliitis	1.46	0.81 to 2.61	0.19			
Arthritis mutilans	2.53	1.07 to 6.01	0.034			
PCS.SF-36	1.03	1.01 to 1.06	0.006	1.08	1.04 to 1.12	<0.001
MCS.SF-36	1.01	0.99 to 1.03	0.21			
HAQ	1.48	0.95 to 2.32	0.08	3.49	1.80 to 6.79	<0.001

BMI, Body Mass Index; HAQ, Health Assessment Questionnaire; MCS.SF-36, mental health factors of quality of life; PCS.SF-36, physical health factors of quality of life.

significant associations with all studied intervals of diagnostic delays (>6 months, >1 and >2 years), which clearly highlights that even a relatively short 6-month delay to diagnosis can lead to poor long-term physical function. There is only one previous study in PsA which has shown that symptom duration of ≥1 year is associated with worse HAQ scores.[11] Fourth, when we studied quality of life using SF-36 scores, we found that delay in receiving rheumatology care of >1 or >2 years was significantly associated with poor physical health factors of quality of life. These are important findings with effects on quality of life not previously examined. Fifth, this study clearly shows that diagnostic delay leads to worse radiographic damage in PsA. There is only one other study in PsA which has shown that radiological damage is more marked in patients presenting with >2 years of disease duration.[12] Our study is unique in showing that even a delay of 6 months from symptom onset is associated with significantly higher odds of having erosions. Moreover, we also noted that the presence of arthritis mutilans, which is considered as the most severe end of PsA-related joint damage, was significantly associated with all studied intervals of the diagnostic delays on univariate analysis (>6 months, >1, >2 years), and was significantly associated with a diagnostic delay of >1 year after adjusting for the confounders.

Finally, achieving drug-free remission which may be viewed as a surrogate for successful rheumatological outcome has significant negative association with a diagnostic delay of >1 year, and a significant positive association with an early rheumatologist encounter of <6 months. This very clearly highlights the benefits of early review and the adverse outcomes associated with the delay in seeing a rheumatologist.

These results suggest that to further improve the outcomes in PsA patients, an important challenge is to get patients with arthritis see a rheumatologist as early as possible after symptom onset. The early identification of patients with PsA among patients with psoriasis therefore assumes considerable importance. Patients with psoriasis are usually managed by GPs or by dermatologists who can either rely on self-reported joint symptoms to identify PsA or be more proactive in elucidating the appropriate musculoskeletal symptoms and signs. Both approaches present difficulties with patients failing to appreciate the relevance of their symptoms and time constraints on GPs and dermatologists that hinder the appropriate assessment. On the other hand, it has also been shown that patient factors are the main cause for delay to accessing care by a rheumatologist.[19] This highlights the importance of raising sufficient patient awareness about inflammatory arthritis.

The strengths of our study include the following: (1) we included a wide range of demographic details, clinical features, PROMs and most of disease activity and severity indices for PsA, which allowed us to investigate more effectively the impact of diagnostic delays; (2) to minimise the selection bias, we have attempted to recruit all consecutive patients attending rheumatology clinics; (3) to standardise the study procedures, all patients were reviewed by a single, trained rheumatologist; (4) since ethnic variation can contribute to diagnostic delays,[20] this study was performed in a relatively homogeneous Irish population (both parents of every studied patient were Irish). We acknowledge that there are some limitations to our study. For example, it was a cross-sectional study and we did not measure the time and reasons why PsA patients delayed consulting their GPs, or the time it took for a GP to decide making a referral and then the time it took for the patient to see the rheumatologist once the referral had been made. Similarly, there is a risk of potential inaccuracy in retrospectively retrieving data from medical notes. Furthermore, since this was a cross-sectional assessment of PsA patients attending rheumatology clinics, it is possible that patients with severe disease tend to attend or continue to receive follow-up at clinics, whereas patients with milder disease might not bother to attend rheumatology clinics.

In conclusion, our study shows that in PsA, even a 6-month delay from symptom onset to the first visit with a rheumatologist can lead to the development of peripheral joint erosions and worse long-term physical function. Moreover, significantly less common drug-free remission and more common arthritis mutilans were noted among patients presenting >1 year after symptom onset. These data clearly suggest that adverse clinical, radiographic, quality of life and physical function outcomes happen early in the disease course and efforts to diagnose patients soon after symptom onset will likely improve outcomes.

Correction notice This article has been corrected since it was published Online First. Changes have been made to the numbers in rows 'DMARDs/TNFi free' and 'No. of DMARDs/TNFi failures' in table 2.

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Competing interests None.

Patient consent Obtained.

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