Determinants of patient and physician global assessment of disease activity and their discrepancies amongst South Africans with Rheumatoid Arthritis

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Dedication

This thesis owes its existence to the unwavering support of numerous individuals, without whom this journey would not have been possible. My heartfelt gratitude goes to my friends and family, with a special mention to Ismail Rishwaan Rashid, for standing by me and offering invaluable support throughout this process.

Declaration

I, Sariu Ali didi declare that this research report is my own work. It is being submitted for the degree of Master of Philosophy in Rheumatology at the University of Cape Town, South Africa. Neither the whole work or any part of it has been submitted before for any degree or examination at this or any other University. This work has not been reported or published prior to registration for the above-mentioned degree.

Signature: Signed by candidate

Date: 10/ 02 /2024

Table of Contents

Abstract

Background: Patient and physician global assessments (PGA and PhGA) play a crucial role in treatment decisions, yet discordance in these assessments is common. Factors influencing PGA and PhGA and discordance in South African (SA) Rheumatoid Arthritis (RA) patients remain poorly understood.

Methods: This cross-sectional study included consenting adults with RA attending a tertiary hospital. Demographic, disease-specific, and patient-reported outcome data were collected. A discordance score was calculated by subtracting the PhGA score from the PGA score, and discordance was defined as PGA-PhGA ≥ 2.5. Determinants of PGA, PhGA, and their discrepancies were explored using correlation analyses, linear regression, and logistic regression.

Results: Of 550 patients, most were female (84.9%), with a mean (SD) age and disease duration of 55.8 (12.9) and 11.5 (9.7) years. Discordance was seen in 27.5%. Pain severity significantly influenced PGA, while tender and swollen joint counts predominantly influenced PhGA. A large portion of the variance in PGA and PhGA (62.0 % and 50.3% respectively) was unexplained. Patients with discordance reported higher pain scores, and problems with usual activities but had lower swollen joint counts and were more likely to be in remission or low disease activity than concordant patients.

Conclusion: Discordance in patient-physician assessments exists in a considerable proportion of SA RA patients. Pain severity and functional limitations greatly influence patient perceptions. Addressing pain and activity limitations could help reduce discordance, optimize disease management, and foster shared decision-making. Further longitudinal and qualitative research is essential for a more comprehensive understanding of our RA patients' perspectives.

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Format and Contributions

This thesis is presented in the publication -ready format. The thesis has been formatted and prepared for the Clinical Rheumatology Journal.

- An Abstract from this research has been submitted to European Alliance of Associations for Rheumatology (EULAR) congress 2023 and has been published in Annals of Rheumatic Diseases

All authors listed below meet the following criteria of the International Committee of Medical Journal Editors (ICMJE). We have itemised their contributions according to the ICMJE criteria below:

- Sariu Ali Didi
    - Overall conception and design of the study, the acquisition of data at Groote Schuur Hospital, interpretation
    - Drafting and critical revising of the work
    - Final approval of the version to be published
    - Agrees to be accountable for all aspects, accuracy and integrity of the work

- B Hodkinson
    - Overall conception and design of the study, the acquisition of data at Groote Schuur Hospital, interpretation
    - Drafting and critical revising of the work
    - Final approval of the version to be published
    - Agrees to be accountable for all aspects, accuracy and integrity of the work

List of Abbreviations

Abbreviation	Definition
ACPA	Anti citrullinated peptide antibody
bDMARD	Biologic disease modifying antirheumatic drug
BMI	Body mass index
CDAI	Clinical Disease activity index
csDMARDs	Conventional synthetic disease-modifying drugs
EQ5D	European quality of life 5 Dimensions
HADS	Hospital Anxiety and Depression scale
HAQ-DI	Health Assessment Questionnaire Disability Index
HDA	High disease activity
LDA	Low disease activity
MDA	Moderate disease activity
PGA	Patient Global Assessment
PhGA	Physician Global Assessment
PIS	Pain interference score
PSS	Pain severity score
RA	Rheumatoid Arthritis
RF	Rheumatoid factor
SES	socioeconomic status
SJC	Swollen Joint count
TJC	Tender joint Count

Publication-ready manuscript

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Determinants of Patient and physician global assessment of disease activity and their discrepancies amongst South Africans with Rheumatoid Arthritis

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Key Words: Patient Global Assessment, Rheumatoid, Rheumatoid Arthritis, Discordance

Determinants of Patient and physician global assessment of disease activity and their discrepancies amongst South Africans with RA

Introduction

The management of Rheumatoid Arthritis (RA) has evolved with the adoption of the “Treat to Target" strategy, aiming for remission or low disease activity [1-3]. Composite disease activity scores, such as the Simplified Disease Activity Index (SDAI), and Clinical Disease Activity Index (CDAI), are used to assess RA disease activity and to classify the disease into high, moderate or low disease activity states to inform treatment decisions which are shared between patient and physician [4]. These scores combine the 28-joint tender and swollen joint counts (TJC and SJC), the patient global assessment (PGA) “*How is your arthritis in the last week*?” scoring between 0 (very good) and 10 (very poor), and physician global assessment (PhGA) scoring between 0 (very good) and 10 (very poor).
The PGA is an important widely used patient-reported outcome measure (PROM), and provides valuable insights into the patient’s perspective on their disease activity. However, it is well recognized that PGA can be influenced by factors including socio-demographic characteristics, fatigue, sleep disturbances, mental health status, and pain. [5-8].

Differences in the patient’s perceptions of disease activity and their physicians’ assessment can be measured by comparing the PGA and the PhGA. The presence of patient-physician discordance in RA has been observed in clinical trials and clinical practice in up to half of patients, with patients generally reporting higher (worse) scores than physicians[9-11]. This discordance can be attributed to the focus of patients and physicians on different aspects of the disease: patients tend to emphasize symptoms and functional limitations, and physicians tend to emphasize objective measures of inflammation including the SJC and serum acute phase reactants [9-16].

Understanding patient-physician discordance in RA is important. Discordance can be considered a “communication gap”, potentially leading to treatment decisions that are not based on shared decision-making. Indeed, discordance has been shown to negatively affect medical care with poor treatment adherence, higher levels of dissatisfaction, and an increased risk of joint damage, and is also associated with impaired health-related quality of life (HRQoL) and decreased work productivity[17-19]. Interestingly, discordance has recently been shown to be associated with a higher grade of musculoskeletal ultrasound synovitis, suggesting that disease activity is underrated by one of the assessors[20] .

Variation in PGA between countries is well described [7].There is a paucity of research specifically examining patient-physician discordance in South Africa (SA). Because of the cultural diversity in SA, factors including language barriers, cultural beliefs, socioeconomic disparities, and healthcare access may influence the communication and understanding between patients and physicians. We anticipate that studying patient-physician discordance may elucidate these specific challenges and guide the development of culturally sensitive and

contextually appropriate interventions to reduce discordance, enhance the doctor-patient relationship, and improve disease management, patient satisfaction, and treatment adherence, leading to better long-term outcomes. Approval for this study was granted from the University of Cape Town Health Research Ethics Committee (HREC 629/2022), and all participants signed informed consent prior to their inclusion in the study.

Patients and Methods:

A cross-sectional study recruiting RA patients attending the arthritis outpatient clinics at a tertiary academic hospital. Consenting adults (≥ 18 years old) meeting the EULAR/ACR 2010 RA Classification Criteria[21] were invited to participate in the study.

Data collection:

Demographic details including age, gender, self-expressed ethnicity, educational level, employment status, smoking status, and living situation were collated. A poor socio-economic setting (SES) was defined using a pooled index if any of the following were present: the highest level of education at primary school or less; more than 7 persons living in the household; clothes washing done by hand (ie no access to washing machine)[22].
Disease-specific information including disease duration, medication, extra-articular manifestations, presence of rheumatoid factor and/or anti-cyclic citrullinated protein antibodies, joint surgery, and comorbidities was collated.

Clinical assessment with the 28-joint TJC, SJC, PGA, and PhGA were collected. The PGA and PhGA were measured on a 2.5-point Likert Scale from 0 (very good), 2.5 (good), 5 (fair), 7.5 (poor) to 10mm (very poor). Disease activity was calculated using the CDAI, and classified into high, moderate, or low disease activity (HDA, MDA, or LDA) based on cut points of 22 and 10 [4].

The following Patient reported Outcome measures (PROM) were completed by patients, with the help of the study coordinator if required: the EuroQol -3 level (EQ-5D-3L) to explore HRQoL, Health Assessment Questionnaire-Disability Index (HAQ-DI) to measure functional disability, Hospital Anxiety and Depression Score (HADS), FACIT -Fatigue Score (FACIT-F) and Brief Pain Inventory(BPI) to assess anxiety and depression, fatigue and pain respectively. [23-28]

PGA and the PhGA Discordance

A discordance score was calculated by subtracting the PhGA score from the PGA score. Patients were categorized as Concordant (score between -2.5 and +2.5), Discordant (score ≥ 2.5) or Negatively Discordant (score < -2.5).

Statistical Analysis

Pearson's correlation coefficients or Spearman's rank correlation coefficients were calculated for continuous variables and ordinal variables to identify factors correlating with PGA and PhGA. Correlation coefficients 0–0.19, 0.2–0.39, 0.40–0.59, 0.6–0.79 and 0.8–1 was considered as very weak, weak, moderate, strong, and very strong correlations respectively [29]. Subsequently, the significant variables identified in univariate correlation were tested in multivariate analyses and further by linear stepwise regression to determine their contribution to PGA and PhGA. The proportion of variability of each outcome explained by each predictor was expressed by the partial R2. The proportions that could not be explained by the variables are presented as 'unexplained'. Analysis of discordant and concordant groups was tested using T-test and Pearson's Chi-Square test. Binomial logistic regression analysis was done with the inclusion of significant variables found in univariate analysis to assess the predictors of discordance. Statistical analyses were conducted using SPSS version 25, and a p-value <0.05 was considered significant.

Results

Of 550 patients, the majority were female (84.9%), with a mean (SD) age and disease duration of 55.8 (12.9) and 11.5 (9.7) years, respectively with 41.3% having longstanding RA (>10 years) (Table 1). A significant proportion (67.4%) were classified as having low SES; 32.7% of patients were smokers and the majority (75.1%) had at least one comorbidity. Most patients were in LDA or remission (47.8%), and the mean (SD) PGA was 4.9 (2.7) with a lower PhGA 3.3 (2.8). The majority of patients (58.3%) were prescribed ≥2 DMARDs concomitantly, 54.7% used low dose corticosteroids (CS) (≤7.5mg /day), and 13 (2.5%) were prescribed a biologic. The mean HAQ-DI score was 1.5 (0.7) suggesting significant physical disability, with global impairment revealed by the EQ-5D (Table 2). A third of patients had significant depression and anxiety, and the majority reported moderate to severe fatigue.

Determinants of PGA and PhGA

The PGA correlated moderately with the pain severity score (PSS), TJC, SJC, and EQ5D Level Sum Score, and weakly with the pain interference score (PIS), HAQ-DI, fatigue, anxiety, and depression scores and with certain EQ5D domains (problems with usual activities, self-care, and mobility) and use of CS, and very weekly with SES (Table 3). There was no correlation with age, disease duration of RA, or number of comorbidities. PhGA was strongly correlated with SJC and TJC and weakly with all PROMs.

Linear stepwise regression showed the PGA was mainly determined by PSS ($B = 0.3$, $R^2 = 0.25$, $p < 0.001$), with contributions from PIS, TJC, SJC, and problem with usual activities presence of FMS and CS use (Figure 1). These variables accounted for 38.0 % of the variance in PGA, with 62.0 % unexplained ($p < 0.001$). The major determinant of PhGA was SJC ($B = 0.5$, $R^2 = 0.43$, $p < 0.001$), which together with TJC, fatigue, and pain explained 49.7% of the variance in PhGA, leaving 50.3% unexplained ($p < 0.001$).

PGA and the PhGA Discordance

Most patients (n=399, 72.6%) and physicians had similar global assessments (Concordant group). Patient-physician discordance occurred in 151 (27.5%) of patients, with 136 patients (24.7%) rating their global assessments worse than their physician (Discordant group). Fifteen patients rated their global assessments better than their physician's “Negatively Discordant”, and this group was excluded from this analysis.

Comparing the Discordant group with the Concordant group revealed significant differences in disease activity and some PROMs (Table 4). Patients in the Discordant group had lower TJC, lower SJC, and lower PhGA, with a higher proportion of patients in the LDA (58.1%) and MDA (32.4%) categories than in the HDA (9.6%) category (p = 0.001). Discordant patients also had a significantly worse EQ5D Level Sum Score, more problems with usual activities, and higher PSS, with a higher prevalence of fibromyalgia. There were no significant differences in age, gender, SES, duration of RA, comorbidities, or presence of osteoarthritis nor in HAQ-DI, anxiety, depression, or fatigue scores between the groups.
Binomial logistic regression analysis showed that patients with lower SJC, high PSS, and problems with usual activities, are more likely to score their disease activity higher than their physician.

Discussion

Our study examined the global assessment of disease activity by patients and physicians, and the discrepancies between them, in indigent South African RA patients. We showed that pain severity had the strongest contribution to the PGA, along with the TJC, SJC, problems with usual activities, and CS use. For the PhGA, the SJC was the most influential factor, with other determinants including TJC, fatigue, and pain. These findings align with studies conducted in various regions, indicating that patients' perceptions of disease activity are influenced by the impact of RA, while physicians focus on objective signs of inflammation.[12-16, 18, 30].

In our study, patient-physician discordance occurred in 27.5% of patients, with 24.7% of patients rating their disease activity higher than their physicians. These results are somewhat lower than rates reported elsewhere, where up to half of patients score their arthritis differently to their physicians.[10, 11, 31] Patients with discordance had poorer PROMs, particularly more problems with usual activities, higher PSS, a higher prevalence of fibromyalgia but notably lower TJC and SJC. The majority of discordant patients were in LDA or MDA states but did not feel they were doing well. Elsewhere, patients with longstanding disease have also been shown to have persistently high PGA scores despite low disease activity, joint counts, and inflammatory markers [17, 32]. Pain and functional disability may have resulted in high PGA scores, even in the absence of joint inflammation[6, 33-36]. Addressing both pain and activity limitations, particularly in patients with low joint counts, may reduce discordance and build a good doctor-patient relationship, leading to increased patient satisfaction with care.

Mental health scores were not associated with discordance in our study although a third of patients had significant anxiety and/or depression, in contrast to findings by Barton et al where higher depressive symptoms were associated with discordance.[37]

There was significant unexplained variability in PGA in this study (62.4%). This is likely due to the subjective nature of PGA, influenced by individual perceptions and expectations together with other unmeasured factors, such as specific disease manifestations and social support. The cross-sectional design and inherent variability in PGA further contribute to this unexplained portion. Further research including qualitative interviews and longitudinal follow-up may allow a better understanding of this variability in PGA.

More than half the patients in our study were using daily low-dose CS. This is an area for improvement, given that most patients were in remission or LDA. In particular, discordant patients with low disease activity using CS require education regarding the toxicity of CS, and better pain management.

The main limitation of our study is the cross-sectional design, which restricts our ability to establish causal relationships and capture disease activity fluctuations over time. Additionally, as a cost-saving measure, we did not measure C-reactive protein (CRP) or other acute phase reactants and relied on the CDAI to assess disease activity [38]. Elsewhere, high CRP levels are associated with discordance.

In conclusion, our study of indigent RA patients with longstanding disease shows that over a quarter of patients rate their disease activity higher than their clinicians, particularly when disease activity is low. Pain severity and functional limitations play a crucial role in patients' assessment of their disease and are areas for intervention to reduce patient-physician discordance to optimize disease management and inform shared treatment decisions. Clinical review (with musculoskeletal ultrasound), pain control strategies, and assessment by occupational and physiotherapists together with exercise may reduce discordance. Additionally, the unexplained variability in PGA highlights the need for further research incorporating a wider range of variables including structural damage, health literacy and patient expectations.

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Conflict of Interest

The authors have no conflict of interest to declare

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List of Tables and Figures

Table 1 Demographic and clinical details of 550 rheumatoid arthritis patients

Demographic details	Age years mean (SD)	55.8 (12.9)
	Duration of RA years mean (SD)	11.5 (9.7)
	Female n (%)	467 (84.9%)
	BMI (Kg/m2) mean (SD)	31.6 (8.3)
	Current Smoker n (%)	180 (32.7)
	Employed n (%)	109 (20.6)
	Work Discontinuation Due to RA	223 (40.5)
	Low SES (pooled Index) n (%)	369 (67.1)
	Sero-positivity ((RF or ACPA) n (%)	403 (91.6)
Disease Activity	CDAI mean (SD)	14.4 (11.9)
	TJC28 mean (SD)	3.1 (4.5)
	SJC28 mean (SD)	3.0 (4.4)
	PGA mean (SD)	4.9 (2.7)
	PhGA mean (SD)	3.3 (2.8)
	Remission n (%)	65 (11.8)
	LDA n (%)	198 (36.0)
	MDA n (%)	166 (30.2)
	HDA n (%)	121 (22.0)
Treatment	1 csDMARD n (%)	202 (39.1)
	≥2csDMARD n (%)	301 (58.3)
	bDMARD n (%)	13 (2.5)
	Prednisone ≤7.5mg/d n (%)	301 (54.7)
	Joint Surgery n (%)	68 (12.6)
Comorbidities	None n (%)	137 (24.9)
	1-2 n (%)	316 (57.5)
	≥3 n (%)	97 (17.6)
	Fibromyalgia Syndrome n (%)	40 (7.3)

Abbreviations: SD-standard deviation ;RA-rheumatoid arthritis; BMI-body mass index; SES-socioeconomic status; RF - rheumatoid factor ; ACPA- anti citrullinated peptide antibody; CDAI-clinical disease activity index; TJC-tender joint count; SJC-swollen joint count; PGA-patient global assessment; PhGA-physician global assessment ; LDA-low disease activity; MDA-moderate disease activity; HDA- high disease activity; csDMARD- conventional synthetic disease modifying antirheumatic drug; bDMARD- biologic disease modifying antirheumatic drug

Table 2. Patient-reported outcomes of 550 patients.

HAQ-DI	Total score mean (SD)	1.5 (0.7)
	Score ≥ 0.5 n (%)	479 (87.1)
EQ5D- 3L:	Level Sum Score mean (SD)	9.3(1.9)
	Problems with Mobility n (%)	357 (64.9)
	Problems with Self-care n (%)	342 (62.2)
	Problems with Usual Activities n (%)	423 (76.9)
	Pain n (%)	342 (62.2)
	Anxiety and depression n (%)	517 (94.0)
Pain	PSS (0-10) mean (SD)	4.7 (2.0)
	Pain interference score (0-10) mean (SD)	4.5 (2.4)
HADS	Anxiety score mean (SD)	8.4 (4.8)
	Anxiety score >11 n (%)	175 (32.2)
	Depression score	9.2 (6.1)
	Depression score >11 n (%)	185 (34.1)
FACIT-Fatigue Score	Total Score mean (SD)	28.7(13.4)
	No fatigue n (%)	147 (26.7)
	Fatigue n (%)	316 (57.4)
	Severe Fatigue n (%)	87 (15.8)

Abbreviations: HAQ-DI-Health Assessment Questionnaire-Disability Index, EQ5D-3L- European Quality of Life-5 Dimension 3 level; PSS-pain severity score, PIS-Pain interference score, HADS- Hospital Anxiety and Depression scale; FACIT-Functional Assessment of Chronic Illness Therapy.

Table 3. Factors influencing the PGA and PhGA —Univariate analysis

		Patient Global Assessment		Physician Global Assessment	
		Correlation Coefficient (95% CI)	**p-value**	**Correlation Coefficient (95% CI)**	**p-value**
Demographics	**Age**	-0.07 (-0.16 to 0.01)	ns	-0.05 (-0.13 to 0.03)	ns
	Duration of RA	-0.07 (-0.16 to 0.01)	ns	-0.015 (-0.10 to 0.07)	ns
	Female	0.09 (0.01 to 0.12)	0.03	0.06 (-0.03 to 0.15)	ns
	Low SES on pooled index	0.09 (0.001 to 0.17)	0.04	0.06 (-0.02 to 0.15)	ns
	Primary school education only	-0.09 (-0.18 to 0.00)	0.05	-0.04 (-0.13 to 0.05)	ns
	Employed	-0.03 (-0.11 to 0.06)	ns	-0.01 (-0.10 to 0.08)	ns
Disease details	**TJC**	0.46 (0.39 to 0.53)	<0.001	0.61 (0.55 to 0.66)	<0.001
	SJC	0.43 (0.36 to 0.49)	<0.001	0.66 (0.61 to 0.71)	<0.001
	No of csDMARDs	0.11 (0.03 to 0.20)	0.012	0.23 (0.15 to 0.31)	<0.001
	Prednisone use	0.16 (0.08 to 0.25)	<0.001	0.21 (0.12 to 0.29)	<0.001
Comorbidities	**No of Comorbidities**	0.04 (-0.05 to 0.12)	ns	-0.06 (-0.15 to 0.02)	ns
	Fibromyalgia	0.12 (0.04 to 0.21)	0.004	-0.01 (-0.10 to 0.08)	ns
	Secondary OA	-0.03 (-0.12 to 0.05)	ns	0.01 (-0.08 to 0.20)	ns
	Previous Joint Surgery	0.02 (-0.07 to 0.10)	ns	0.02 (-0.07 to 0.10)	ns
EQ5D	**LSS**	0.40 (0.33 to 0.47)	<0.001	0.28 (0.20 to 0.26)	<0.001
	Problem with usual activity	0.32 (0.24 to 0.39)	<0.001	0.16 (0.08 to 0.25)	<0.001
	Problem with mobility	0.25 (0.16 to 0.33)	<0.001	0.20 (0.12 to 0.28)	<0.001
	Problem with Self Care	0.25 (0.17 to 0.33)	<0.001	0.19 (0.11 to 0.27)	<0.001
HAQ-DI	**HAQ-DI**	0.32 (0.24 to 0.39)	<0.001	0.26 (0.19 to 0.34)	<0.001
	PSS	0.50 (0.43 to 0.56)	<0.001	0.34 (0.26 to 0.41)	<0.001
	Pain interference score	0.37 (0.30 to 0.44)	<0.001	0.26 (0.18 to 0.34)	<0.001
FACIT-F	**FACIT-F score**	-0.27 (-0.35 to -0.19)	<0.001	-0.24 (-0.31 to -0.16)	<0.001
HADS	**Depression**	0.28 (0.20 to 0.36)	<0.001	0.24 (0.21 to 0.37)	<0.001
	Anxiety	0.25 (0.17 to 0.33)	<0.001	0.21 (0.13 to 0.29)	<0.001

Data represent Pearson's correlation coefficient (r) or Spearman's rank correlation coefficient (ρ) for the Patient Global Assessment and the Physician Global Assessment

Abbreviations: RA-Rheumatoid arthritis; SES-Socioeconomic status; TJC- Tender joint count; SJC- Swollen joint count; csDMARD -Conventional synthetic disease modifying antirheumatic drugs; OA-Osteoarthritis ; EQ5D LSS -European Quality of Life-5 Dimension; LSS- Level Sum Score; HAQ-DI -Health Assessment Questionnaire-Disability Index; PSS - pain severity score; FACIT-Functional Assessment of Chronic Illness Therapy – Fatigue Scale; HADS- Hospital Anxiety and Depression scale.

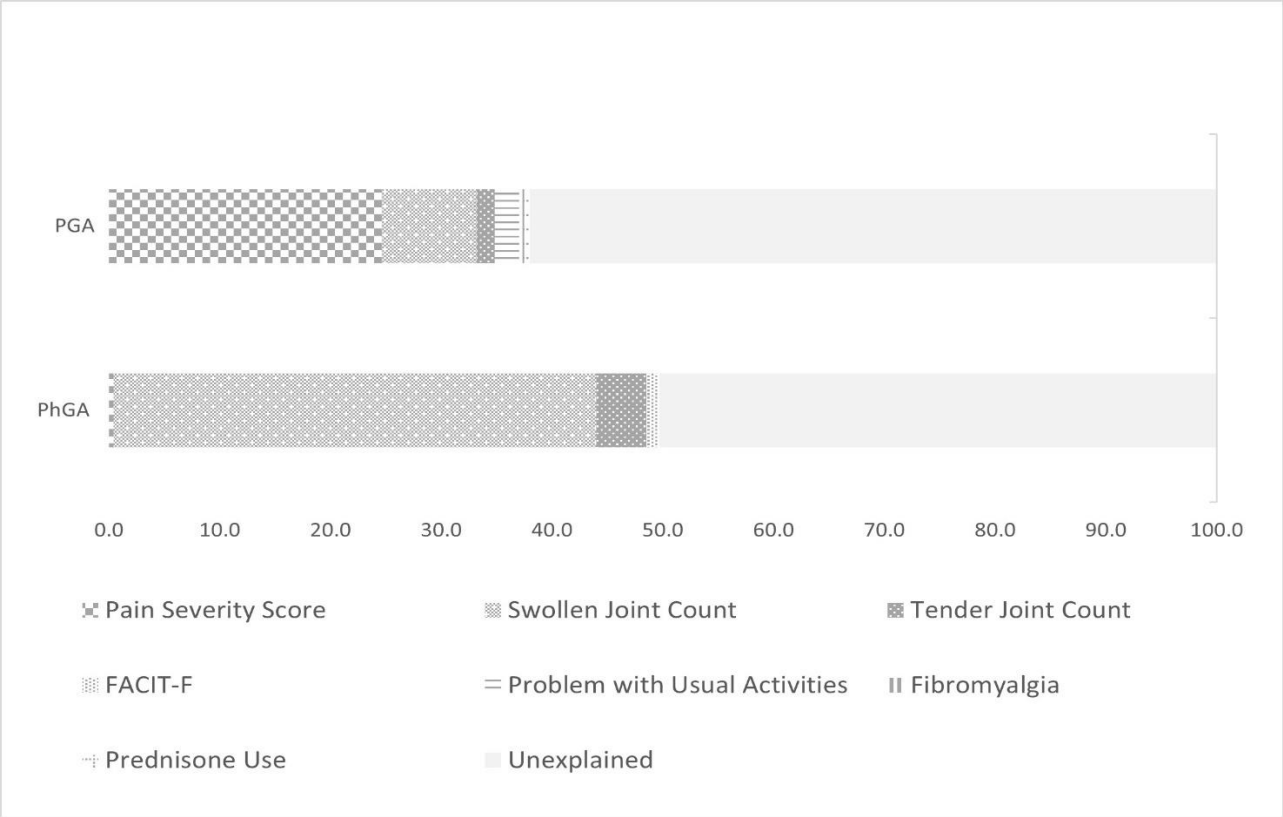


Figure 1. Contributors of PGA and PhGA by linear stepwise regression

Table 4. Comparison of Concordant (PGA-PhGA -2.5 to2.5) and Discordant Group (PGA-PhGA >2.5)

	Univariate Analysis			Multivariate Analysis	
	Concordant group n= 399	Discordant group n= 136	p-value	Exp(B) (95% CI)	p-value
Age (years)- mean (SD)	55.7(13.3)	55.8(11.6)	ns		
Female- n (%)	334(83.7)	119(87.5)	ns		
Low Socio-Economic Status n (%)	260(65.2)	96(70.6)	ns		
Duration of RA (years) mean (SD)	11.7 (10.1)	10.7 (8.1)	ns		
Tender joint count mean (SD)	3.47 (4.7)	1.9 (3.0)	<0.001		
Swollen joint count mean (SD)	3.5(4.6)	1.3(2.7)	<0.001	0.82 (0.74-0.91)	<0.001
Physician global assessment mean (SD)	3.8(2.8)	1.7(1.7)	<0.001		
Patient global assessment mean (SD)	4.4 (2.7)	6.6 (1.9)	<0.001		
CDAI mean (SD)	12 (5-22.5)	9 (7-14)	ns		
Remission/ Low Disease Activity n (%)	181 (45.4)	79 (58.1)			
Moderate Disease Activity n (%)	116 (29.1)	44(32.4)	<0.001*		
High Disease Activity n (%)	102(25.6)	13(9.6)			
Prednisone Use n (%)	357 (89.5)	118(86.8)	ns		
No of comorbidities mean (SD)	1.4 (1.2)	1.8 (1.2)	ns		
Comorbidities ≥3 n (%)	67 (16.8)	29 (21.3)	ns		
Fibromyalgia n (%)	22 (5.5)	17(12.5)	0.007		
Secondary OA n (%)	43 (10.8)	11 (8.1)	ns		
Previous Joint Surgery n (%)	48 (12.4)	17 (12.5)	ns		
HAQ-DI mean (SD)	1.49(0.72)	1.54 (0.71)	ns		
EQ5D-3L- Level Sum Score	9(8-11)	10(9-11)	0.024		
Problems with Mobility n (%)	252(63.2)	96(70.6)	ns		
Problems with selfcare n (%)	244(61.2)	90(66.2)	ns		
Problems with Usual Activities n (%)	293(73.4)	122(89.7)	<0.001	3.05 (1.62- 5.75)	<0.001
PSS mean (SD)	4.6(2.1)	5.2(1.8)	0.005	1.22 (1.09-1.38)	<0.001
Pain interference score	4.4(2.5)	4.8(2.2)	0.08		
HADS-Anxiety Score	8.2(4.7)	8.9(4.8)	ns		
HADS-Depression Score mean (SD)	8.9(6.0)	9.7(6.2)	ns		
FACIT-F scale mean (SD)	28.6(13.5)	27.9(12.5)	ns		

* p-value obtained from chi-square comparing the three groups.

Abbreviations: RA-rheumatoid arthritis; CDAI- Clinical Disease Activity Index; OA- osteoarthritis; HAQ-DI -Health Assessment Questionnaire-Disability Index; EQ5D -European Quality of Life-5 Dimension; PSS - pain severity score; HADS- Hospital Anxiety and Depression scale; FACIT-F- Functional Assessment of Chronic Illness Therapy – Fatigue Scale.

Appendix A – Clinical Resource Items

PATIENT INFORMATION:

Dear Patient

I am Professor Bridget Hodkinson and would like to invite you to take part in our Rheumatoid Arthritis study. We would like to collect information about your Rheumatoid Arthritis and how it affects your life so that we can understand our patients and their needs, and so that we can develop studies or offer help so that you get the best care and the best outcomes living with your illness.

What is involved?

Your doctor will record details about you (your age, gender and postal code), and about your Rheumatoid Arthritis (diagnosis, date of diagnosis and medications you are using). We would also like to understand your physical function, pain, energy levels and mental health and will ask you to complete a 1-2 page questionnaire on each of these topics. These questionnaires will take 20-30 minutes of your time, and you will be able to complete them while you are waiting to be seen by your doctor. You may feel that some of the questions are intrusive or difficult to answer – you are free to leave these questions blank, or discuss with the study nurse or doctor.

The collected information would then be registered on a computer database. This database will not entail any extra visits over and above normal care. You will not be receiving any experimental therapies. There are no risks, nor are there any direct benefits to you if you agree to join the study. There may be benefit to society in the long term as we improve our understanding of rheumatic diseases and develop strategies and studies to improve the lives of our patients.

What if I do not wish to take part in this study?

All registries and studies are always completely voluntary. If you do not wish to take part this will not affect the treatment you receive. All the information collected will be handled in a strictly confidential manner and the results will only be used for research purposes. You can withdraw from this database at any time.

Other information

All your written and computer records will be kept strictly private and confidential at all times. Data Protection Act regulations have been complied with to ensure confidentiality. There will not be personal identification in any reports on this study.

IF YOU HAVE ANY FURTHER QUESTIONS ABOUT THE DATABASE, PLEASE CONTACT:

Principal Investigator: Prof Bridget Hodkinson telephone:021 404 2131

Ethics Committee Chairman Prof Blockman telephone 021 650 5057

INFORMED CONSENT

1. I have read the patient information sheet regarding the above study and have had the opportunity to discuss the details with _____and to ask questions. I understand fully what is to be done.
2. I have agreed to take part in the study as it has been explained to me, but I understand that I am completely free to withdraw from the study or any part of the study at any time I wish, without prejudice to my further treatment.
3. I understand that this study is designed to promote medical knowledge and may not benefit me personally.
4. I understand that the results of the study may be published if a research project is done, but my personal results will remain confidential, and my name will not be disclosed in any report. I understand that my family doctor will be notified of my participation in this study and that any results, which might be relevant to my medical care, will be forwarded onto my family doctor.

I hereby fully and freely consent to participate in the study, which has been fully explained to me.

Signature of patient, _____

Name of patient (Print) _____ Date_____

I confirm that I have explained to the volunteer named above, the nature and purpose of the tests to be undertaken.

Signature Rheumatologist or Rheumatology Nurse

_____

Name _____ Date_____

(APPENDIX 1) Data Collection Forms

DATE of entry: ____/____/____
Contact number : _____

Email address: _____

SEX: M F **ETHNICITY:** B C A W

Sticker or NAME: _____

HOSPITAL NO: _____

Date of Birth _____

Postal code _____

Weight (kg)_____ **Height** (cm)_____ **Waist circumference** (cm) _____

Year of Rheum symptom onset: _____ **At GSH Rheum since** _____

Rheumatology Diagnosis: ☐ ANCA vasculitis ☐ Axial spondyloarthritis ☐ AOSD ☐ FMS ☐ Gout
☐ Juvenile idiopathic arthritis ☐ Inflammatory myositis ☐ HIV arthropathy ☐ MCTD
☐ Polymyalgia rheumatica ☐ Psoriatic arthritis ☐ Rheumatoid arthritis ☐ SLE
☐ Systemic sclerosis ☐ Sjogren's syndrome ☐ Takayasu ☐ Axial SpA ☐ Other SpA
☐ Other _____

Family history (of rheum disease)? ☐ No ☐ Yes **Details** _____

Comorbidities (cross or leave blank):

HT | DM | Dyslipidaemia | Renal dysfunction | COPD | IHD or CCF | Obesity
HYPOTHYROID | HYPERTHYROID | STROKE | PERIPH VASCULAR | Inflam bowel disease
TB | HIV | Hep B | Hep C | NASH | DEPRESSION | Valvular heart dis | FMS
MALIGNANCY IF y details.. | COVID-19

Smoker Y N EX **Highest level of Education** PRIMARY SECONDARY TERTIARY

Work (current or last job) _____

Work Status EMP UNEM Disability grant Old age pension **Stopped work d/t rheum illness?** Y N

How do clothes get washed in your home?
☐ By hand ☐ Washing machine at home ☐ Washing machine in neighbourhood ☐ Laundromat

Who does the clothes washing?
Self Family member Domestic helper

RHEUMATOID ARTHRITIS

cross if involved (ever), blank means not involved

Complications of RA

nodules	scleritis	CQ maculopathy	Sicca symptoms	ILD
myelopathy	Carpal tunnel	Osteoporosis	Pyoderma gangrenosum	

Other _____

Antibodies (ever) RF CCP ANA

Joint surgery:

Date, procedure _____

Date, procedure _____

Date, procedure _____

Medication for RA (ever used?)

MTX CQ SASP LEF RITUX TNFi

OTHER _____

Medication for RA (CURRENTLY used?)

MTX CQ SASP LEF RITUX TNFi

Highest prednisone dose in last 12 months (mg/day)_____

Prednisone dose now (mg/day) _____

Tender Joint Count _____

Swollen Joint Count _____

Physician Global Assessment _____

Patient Global Assessment _____

Rheumatic Disease Unit

Hospital Anxiety and Depression Scale (HADS)

Groote Schuur Hospital

Instructions: Doctors are aware that emotions play an important part in most illnesses. If your doctor knows about these feelings he or she will be able to help you more. This questionnaire is designed to help your doctor know how you feel. Read each item and circle the reply which comes closest to how you have been feeling in the past week. Don't take too long over your replies: your immediate reaction to each item will probably be more accurate than a long thought out response.

I feel tense or 'wound up':	**A**
Most of the time	3
A lot of the time	2
Time to time, occasionally	1
Not at all	0

I still enjoy the things I used to enjoy:	**D**
Definitely as much	0
Not quite so much	1
Only a little	2
Not at all	3

I get a sort of frightened feeling like something awful is about to happen:	**A**
Very definitely and quite badly	3
Yes, but not too badly	2
A little, but it doesn't worry me	1
Not at all	0

I can laugh and see the funny side of things:	**D**
As much as I always could	0
Not quite so much now	1
Definitely not so much now	2
Not at all	3

Worrying thoughts go through my mind:	**A**
A great deal of the time	3
A lot of the time	2
From time to time but not too often	1
Only occasionally	0

I feel cheerful:	**D**
Not at all	3
Not often	2
Sometimes	1
Most of the time	0

I can sit at ease and feel relaxed:	**A**
Definitely	0
Usually	1
Not often	2
Not at all	3

I feel as if I am slowed down:	**D**
Nearly all of the time	3
Very often	2
Sometimes	1
Not at all	0

I get a sort of frightened feeling like 'butterflies in the stomach':	**A**
Not at all	0
Occasionally	1
Quite often	2
Very often	3

I have lost interest in my appearance:	**D**
Definitely	3
I don't take as much care as I should	2
I may not take quite as much care	1
I take just as much care as ever	0

I feel restless as if I have to be on the move:	**A**
Very much indeed	3
Quite a lot	2
Not very much	1
Not at all	0

I look forward with enjoyment to things:	**D**
A much as I ever did	0
Rather less than I used to	1
Definitely less than I used to	3
Hardly at all	2

I get sudden feelings of panic:	**A**
Very often indeed	3
Quite often	2
Not very often	1
Not at all	0

I can enjoy a good book or radio or TV programme:	**D**
Often	0
Sometimes	1
Not often	2
Very seldom	3

Questions relating to anxiety are indicated by an 'A' while those relating to depression are shown by a 'D'. Scores of 0-7 in respective subscales are considered normal, with 8-10 borderline and 11 or over indicating clinical 'caseness'

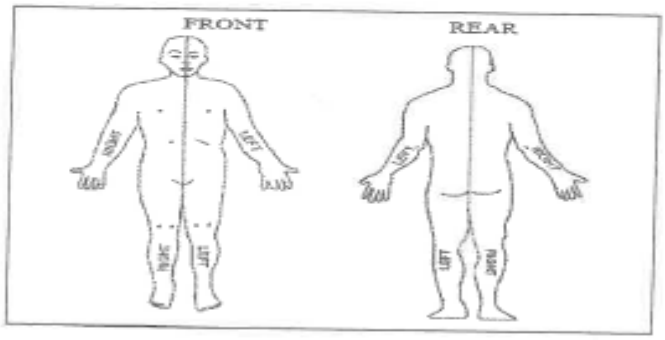
BRIEF PAIN QUIESTIONNAIRE

Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains and toothaches)

1. **Have you had pain other than these everyday kinds of pain today?**
   PLEASE TICK

   Yes ☐ **No** ☐

2. **On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.**



3. **Please rate your pain by circling the number that best describes your pain at it's WORST in the last 24 hours.**
   CIRCLE A NUMBER

No pain 0 1 2 3 4 5 6 7 8 9 10 **Pain as bad as you can imagine**

4. **Please rate your pain by marking circling the number that best describes your pain at it's LEAST in the last 24 hours.**
   CIRCLE A NUMBER

No pain 0 1 2 3 4 5 6 7 8 9 10 **Pain as bad as you can imagine**

5. **Please rate your pain by circling the number that best describes your pain on the AVERAGE .**
   CIRCLE A NUMBER

No pain 0 1 2 3 4 5 6 7 8 9 10 **Pain as bad as you can imagine**

6. **Please rate your pain by circling the number that tells how much pain you have RIGHT NOW.**
   CIRCLE A NUMBER

No pain 0 1 2 3 4 5 6 7 8 9 10 **Pain as bad as you can imagine**

7. **What treatment or dedications are you receiving for your pain?**

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please circle the percentage tha most shows how much RELIEF you have received.

CIRCLE A NUMBER

No Relief — Complete Relief

0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%

9. Circle the number that describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

CIRCLE A NUMBER

Does not interfere — Completely Interferes

0 1 2 3 4 5 6 7 8 9 10

B. Mood

CIRCLE A NUMBER

Does not interfere — Completely Interferes

0 1 2 3 4 5 6 7 8 9 10

C. Walking ability

CIRCLE A NUMBER

Does not interfere — Completely Interferes

0 1 2 3 4 5 6 7 8 9 10

D Normal Work (Includes both work outside the home and housework)

CIRCLE A NUMBER

Does not interfere — Completely Interferes

0 1 2 3 4 5 6 7 8 9 10

E. Relations with other people

CIRCLE A NUMBER

Does not interfere — Completely Interferes

0 1 2 3 4 5 6 7 8 9 10

F. Sleep

CIRCLE A NUMBER

Does not interfere — Completely Interferes

0 1 2 3 4 5 6 7 8 9 10

G. Enjoyment of life

CIRCLE A NUMBER

Does not interfere — Completely Interferes

0 1 2 3 4 5 6 7 8 9 10

FACIT Fatigue Scale

Below is a list of statements that other people with your illness have said are important.

Please circle or mark one number per line to indicate your response as it applies to the past 7 days.

	Not at all	A little bit	Somewhat	Quite a bit	Very much
1) I feel fatigued	0	1	2	3	4
2) I feel weak all over	0	1	2	3	4
3) I feel listless ("washed out")	0	1	2	3	4
4) I feel tired	0	1	2	3	4
5) I have trouble starting things because I am tired	0	1	2	3	4
6) I have trouble finishing things because I am tired	0	1	2	3	4
7) I have energy	0	1	2	3	4
8) I am able to do my usual activities	0	1	2	3	4
9) I need to sleep during the day	0	1	2	3	4
10) I am too tired to eat	0	1	2	3	4
11) I need help doing my usual activities	0	1	2	3	4
12) I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
13) I have to limit my social activity because I am tired	0	1	2	3	4

EQ5d Questionnaire

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today

1) Mobility

I have no problems in walking about

I have some problem in walking about

I am confined to bed

2) Self-Care

I have no problem with self-care

I have no problem washing or dressing myself

I am unable to wash or dress myself

3) Usual Activities (e.g. work, study, housework, family or leisure activities)

I have no problems with performing my usual activities

I have some problems with performing my usual activities

I am unable to perform my usual activities

4) Pain/Discomfort

I have no pain or discomfort

I have moderate pain or discomfort

I have extreme pain or discomfort

5) Anxiety/Depression

I am not anxious or depressed

I am moderately anxious or depressed

I am extremely anxious or depressed

HEALTH ASSESSMENT QUESTIONNAIRE

We are interested in learning how your illness affects your ability to function in daily life

Please place an "x" in the box which best describes your abilities OVER THE PAST WEEK:

	WITHOUT ANY DIFFICULTY	WITH SOME DIFFICULTY	WITH MUCH DIFFICULTY	UNABLE TO DO
DRESSING & GROOMING				
Are you able to:				
Dress yourself, including shoelaces and buttons?	☐	☐	☐	☐
Shampoo your hair?	☐	☐	☐	☐
ARISING				
Are you able to:				
Stand up from a straight chair?	☐	☐	☐	☐
Get in and out of bed?	☐	☐	☐	☐
EATING				
Are you able to:				
Cut your own meat?	☐	☐	☐	☐
Lift a full cup or glass to your mouth?	☐	☐	☐	☐
Open a new milk carton?	☐	☐	☐	☐
WALKING				
Are you able to:				
Walk outdoors on flat ground?	☐	☐	☐	☐
Climb up five steps?	☐	☐	☐	☐
HYGIENE				
Are you able to:				
Wash and dry your body?	☐	☐	☐	☐
Take a tub bath?	☐	☐	☐	☐
Get on and off the toilet?	☐	☐	☐	☐
REACH				
Are you able to:				
Reach and get down a 5 pound object (such as a bag of sugar) from above your head?	☐	☐	☐	☐
Bend down to pick up clothing from the floor?	☐	☐	☐	☐
GRIP				
Are you able to:				
Open car doors?	☐	☐	☐	☐
Open previously opened jars?	☐	☐	☐	☐
Turn faucets on and off?	☐	☐	☐	☐
ACTIVITIES				
Are you able to:				
Run errands and shop?	☐	☐	☐	☐
Get in and out of a car?	☐	☐	☐	☐
Do chores such as vacuuming or yard work?	☐	☐	☐	☐

Appendix B Ethics Approval

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room 45 E-52-E-Floor- Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6492
Email: hrec-submissions@uct.ac.za
Website: www.health.uct.ac.za/home/human-research-ethics

28 November 2022

HREC REF: 629/2022

Prof B Hodkinson
Department of Medicine
OMB
Email: drbridget@gmail.com
Student: sariualididi@gmail.com

Dear Prof Hodkinson

PROJECT TITLE: DISCORDANCE BETWEEN THE PATIENT AND PHYSICIAN ASSESSMENTS OF DISEASE ACTIVITY AMONGST RHEUMATOID ATHRITIS PATIENTS IN THE WESTERN CAPE-9MPHIL CANDIDATE-DR SARIU ALI DIDI)

Thank you for your response letter, addressing the issues raised by the Faculty of Health Sciences Human Research Ethics Committee (HREC).

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30 November 2023.

Please submit a progress form, using the standardised Annual Report Form (FHS016) if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

The HREC acknowledge that the student: Dr Sariu Didi will also be involved in this study.

Please quote the HREC REF 629/2022 in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Please note that for all studies approved by the HREC, the principal investigator **must** obtain appropriate institutional approval, where necessary, before the research may occur.

Yours sincerely

PROFESSOR M BLOCKMAN
CHAIRPERSON, FACULTY OF HEALTH SCIENCES HUMAN RESEARCH ETHICS COMMITTEE

Federal Wide Assurance Number: FWA00001637. Institutional Review Board (IRB) number: IRB00001938 NHREC-registration number: REC-210208-007

HREC/ref 629.2022

Appendix C – Instruction to Authors

Clinical Rheumatology
Journal of the International League of Associations for Rheumatology

Instruction to the Authors

Instructions for Authors

Clinical Rheumatology endorses complete and transparent reporting of biomedical and clinical research. Depending on the study, we recommended the authors to adhere to the relevant EQUATOR Network reporting guidelines when preparing their manuscript.

Types of papers

- **Original Research articles**: word limit 4000 words, 45 references, no more than 6 figures/tables; abstracts must be structured as specified below. After the abstract, include key-points (min. of 1, max. of 4) presented in brief sentences, highlighting the contributions of the paper.

Please note: **It is mandatory that abstracts for Original Research articles adopt the below structure (150-250 words):**• Introduction / objectives – specify the context of the problem (optional), the research aim, question or purpose, and the tested hypothesis.• Method – specify the design of the study, selection criteria of patients, main outcome variable and statistical approach used to test the primary hypothesis.• Results – summarise the main results, present the results that support the hypothesis stated in Introduction providing results in numbers, not just p-values or interpretations, and other relevant results (optional).• Conclusions – summarise what the findings might imply, and the implications and recommendations for future research; conclusions should be coherent with the objectives and the results presented in the abstract.

- **Review articles**: Provide accessible, authoritative, and balanced overviews of a field or topic. Abstract (unstructured, 150-250 words, please avoid using abbreviations and references); 4-6 keywords (please note that the word count refers to individual MeSH words representing the main content of the article); up to 4 key-points; up to 100 references; up to 5 Tables/figures, not including supplementary material. Word limit: 5,000 words.
- **Brief report** 2000 word limit, 25 references, no more than four figures; include key points (minimum of 1, maximum of 4) presented in short sentences, highlighting the contributions of the article. Each manuscript must be formatted as an original article, including a structured abstract.
- **Clinical Image**: Clinical Images are a brief clinical report describing a unique image. All Clinical Images must have patient consent for publication, and the copyright form must be sent with your submission to Clinical Rheumatology, including:• Title page• Structured text including two sections: Presentation (case narrative); Discussion (brief, concise messages).• References (up to 5)• Figure (up to 1, not including supplementary material). Make sure that the figure complies with the image quality standards described in the Clinical Rheumatology instructions for authors section (artwork).• Word count: Up to 300. Provide a figure footnote that is not redundant with the main text.
- **Letters of Biomedical and Clinical Research**: word limit 650 words, 10 references, 2 tables or figures and a discussion; summaries and supplementary material should not be included. Should present advances in highly focused, original clinical and biomedical research that is easily replicable.

- **Perspectives in Rheumatology**: word limit 3500 words, 40 references, no more than 3 figures. Should share a clinical, methodological, scientific, or ethical point of view regarding provocative or hot topics emerging in the clinical practice of rheumatology. Unstructured abstract.
- **Case Based Review**: a case report of extreme clinical interest incorporating a mini review in an area of new knowledge. Word limit 3500 words, 50 references, no more than 5 figures.
- **Letters to editor**: up to 600 words
- **Editorial**: up to 1500 words

Please note:

- **Case Reports** are no longer accepted in the journal.
- **Translated questionnaires** can only be included in *Clinical Rheumatology* articles if permission to use the questionnaire has been granted by the copyright holder.
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