RHEUMATOLOGY

Concise report

doi:10.1093/rheumatology/kex211

Drivers of patient global assessment in patients with rheumatoid arthritis who are close to remission: an analysis of 1588 patients

Ricardo J. O. Ferreira[1,2], Maxime Dougados[3,4,5], John R. Kirwan[6], Cátia Duarte[7,8], Maarten de Wit[9,10], Martin Soubrier[11], Bruno Fautrel[12,13,14], Tore K. Kvien[15], José A. P. da Silva[7,8]* and Laure Gossec[12,13]*, on behalf of the CoimbRA investigators, RAID investigators and COMEDRA investigators

Abstract

Objectives. ACR/EULAR Boolean remission in RA is frequently not obtained solely due to a patient global assessment (PGA) >1/10 (a condition often designated as near-remission). This study aimed to assess which domains of impact could explain an elevated PGA in near-remission patients.

Methods. We performed an ancillary analysis of data from three cross-sectional studies in patients with established RA. Three disease activity states were defined: remission (tender and swollen joint counts, CRP and PGA all ⩽1), near-remission (tender and swollen joint counts, and CRP are all ⩽1 but PGA >1) and non-remission. Physical and psychological domains were assessed using the RA Impact of Disease 0–10 (numeric rating scale) as explanatory factors of PGA. Univariable and multivariable linear regression analyses were performed to explain PGA.

Results. A total of 1588 patients (79.1% females) were analysed. The mean disease duration was 13.0 years (S.D. 9.8) and the 28-joint DAS with four variables was 3.2 (S.D. 1.4). Near-remission [mean PGA 3.6 (S.D. 1.9)] was more frequent (19.1%) than remission (12.3%). Scores of RA Impact of Disease domains were similar in near-remission and non-remission patients. In near-remission, PGA was explained ($R^2_{adjusted} = 0.55$) by pain ($\beta = 0.29$), function ($\beta = 0.23$), physical well-being ($\beta = 0.19$) and fatigue ($\beta = 0.15$).

Conclusion. Near-remission was more frequent than remission. These patients, despite having no signs of significant inflammation, report an impact of disease similar to the non-remission patients. PGA in near-remission seems to be driven by physical rather than psychological domains. Selecting the best therapy for these patients requires a better understanding of the meaning of PGA, both globally and in individual patients.

Key words: rheumatoid arthritis, patient global assessment, patient reported outcomes, disease activity, remission, near-remission, psychological distress, psychological factors, outcomes, disease impact

CLINICAL SCIENCE

[1]Department of Rheumatology, Centro Hospitalar e Universitário de Coimbra, [2]Health Sciences Research Unit: Nursing (UICiSA:E), Nursing School of Coimbra (ESEnfC), Coimbra, Portugal, [3]Faculty of Medicine, Paris Descartes University, [4]Department of Rheumatology, AP-HP, Hôpital Cochin, [5]INSERM (U1153), Clinical Epidemiology and Biostatistics, PRES Sorbonne Paris-Cité, Paris, France, [6]Academic Rheumatology Unit, Bristol Royal Infirmary, University of Bristol, Bristol, UK, [7]Department of Rheumatology, Centro Hospitalar e Universitário de Coimbra, [8]Clínica Universitária de Reumatologia, Faculty of Medicine, University of Coimbra, Coimbra, Portugal, [9]Patient Research Partner, EULAR Standing Committee of People with Arthritis/Rheumatism in Europe (PARE), Zurich, Switzerland, [10]Department of Medical Humanities, VU University Medical Centre, Amsterdam, The Netherlands, [11]Department of Rheumatology, CHU Clermont-Ferrand, Clermont-Ferrand, [12]Faculty of Medicine, UPMC University Paris 06, GRC-UPMC 08 (EEMOIS), [13]Department of Rheumatology, AP-HP, Pitié Salpêtrière Hospital, Paris, [14]CRI IMIDIATE, French Clinical Research Infrastructure Network, Toulouse, France and [15]Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway

Submitted 12 October 2016; revised version accepted 25 April 2017

*José A. P. da Silva and Laure Gossec contributed equally to this study.

Correspondence to: Ricardo Jorge de Oliveira Ferreira, Serviço de Reumatologia, Consulta Externa, Piso 7, Centro Hospitalar Universitário de Coimbra, EPE, Avenida Dr. Bissaya Barreto, 3000-075 Coimbra, Portugal.
E-mail: ferreira.rjo@gmail.com

Rheumatology key messages

- One-third of RA patients fail to reach remission solely because of patient global assessment (near-remission).
- In near-remission RA patients, significant disease impact may persist despite the absence of signs of inflammation.
- High patient global assessment in near-remission reflects both psychological and physical aspects of the disease impact of RA.

Introduction

Disease remission (or at least low disease activity) is the therapeutic target for patients with RA in current treatment recommendations [1, 2]. Remission is defined according to the ACR/EULAR criteria [3], which in the Boolean-based definition require that the 28 tender joint count (TJC28), 28 swollen joint count (SJC28), CRP (mg/dl) and patient global assessment (PGA; 0–10 scale) are all $\leqslant 1$.

The condition where patients fail to reach remission solely because of PGA has been designated as near-remission [4]. These patients have no signs of significant joint inflammation since joint counts and CRP are $\leqslant 1$, but they evaluate their disease (using PGA) as $> 1/10$. In published studies, 21–31% of RA patients were in near-remission [4–6]. Following current treatment recommendations [1, 2], this state of near-remission could justify reinforcement of immunosuppressive therapy. However, this may not be the best choice if the reason for not achieving remission is not inflammatory activity. In these cases, adjuvant therapies such as analgesics, anti-depressants or self-management programs might be more appropriate. To select the best intervention in such cases, it is essential to understand why patients without signs of significant inflammatory activity do not achieve a PGA $\leqslant 1$.

In RA patients, PGA appears to be influenced by not only RA disease activity, but also by sociodemographic features, country/culture, psychological factors and comorbidities, with emphasis on FM [7]. However, no data are available on the meaning of PGA in the specific condition of near-remission.

The aims of this study were to assess which domains of impact may explain the elevated PGA in near-remission patients and to assess which domains of health better discriminate between disease activity states.

Methods

Study design and setting

This was an ancillary analysis of three studies of patients with established RA: baseline data from the RA Impact of Disease (RAID) elaboration database [8], an international (12 European countries) observational study in 2008–09; baseline data from COMorbidities, EDucation in Rheumatoid Arthritis (COMEDRA) trial [9], a French multicentre clinical trial in 2011; and the Coimbra RA cohort (CoimbRA), a Portuguese, cross-sectional observational study in 2015 [10].

Participants

In all three studies consecutive adult patients were included if they had definite RA (ACR 1987 revised criteria or ACR/EULAR 2010 classification criteria) and were able to complete questionnaires. For COMEDRA, additional inclusion criteria were age <80 years, stable disease (for at least 3 months) and having no planned surgery in the 6 months following the study baseline. Written consent was obtained according to the Declaration of Helsinki for all studies, as well as approval from ethical committees, as previously reported [8–10]. Additional approval for this ancillary study was not required. Here, patients were analysed if they had RAID [8] and remission components available [3].

PGA

PGA was assessed in the three studies using the same formulation [3]—considering all the ways your arthritis has affected you, how do you feel your arthritis is today?—using either a 0–100 visual analogue scale or a 0–10 numeric rating scale (in COMEDRA).

Remission definitions

Four different Boolean-based concepts of remission were used in this study: the ACR/EULAR Boolean remission [TJC28, SJC28, CRP (mg/dl) and PGA, all $\leqslant 1$] [3]; near-remission [TJC28, SJC28 and CRP (mg/dl) all $\leqslant 1$ and PGA >1]; non-remission [TJC28 or SJC28 or CRP (mg/dl) >1, irrespective of PGA] and three-variable (3v) remission [11] [TJC28, SJC28 and CRP (mg/dl) all $\leqslant 1$; PGA excluded from consideration].

Explanatory factors of PGA

The seven domains of the RAID score [8] were used as possible factors to explain PGA: that is, physical (pain, function and physical well-being), psychological (emotional well-being and coping/self-efficacy) and mixed domains (fatigue and sleep) [12]. Each domain is assessed by a numeric rating scale, ranging from 0 (no impact) to 10 (high impact).

Other data collection

Age, gender, disease duration, current biologic agent (yes/no), HAQ, physician's global assessment and 28-joint DAS with 4 variables (DAS28-4v) were also assessed for patient's characterization.

Statistical analyses

Descriptive analyses, Student's *t*-test comparing disease activity states and Hedges' g for effect size (ES) were performed using SPSS Statistics version 20.0 software (IBM, Armonk, NY, USA). The ES assessed the discriminant capacity of impact domains to distinguish the disease activity states. To determine the drivers of PGA in near-

remission patients, univariable (Pearson's correlation coefficient) and multivariable analyses (linear regression, backward method) were used.

Results

Patient characteristics

The evaluable population comprised 1588 patients (RAID = 348, COMEDRA = 936, CoimbRA = 304) who presented with typical established RA with long disease duration (Table 1). Patients from COMEDRA and RAID were often treated with biologic disease-modifying drugs (74.7% and 50.0%, respectively). Disease activity was, on average, low in COMEDRA and in CoimbRA and moderate in RAID (Table 1). All aspects of disease impact presented mean values of ~3.5 on 0–10 scales, except for fatigue [mean 4.3 (S.D. 2.8)], where higher numbers reflect worst status (Table 1).

Remission rates and PGA cut-offs

ACR/EULAR Boolean-based remission was achieved by only 195 (12.3%) patients (6.0% in RAID, 15.6% in COMEDRA and 9.2% in CoimbRA). Overall, 303 (19.1%) patients were in near-remission (14.4% in RAID, 14.6% in COMEDRA and 38.2% in CoimbRA). Near-remission was at least as frequent as remission (COMEDRA) and up to four times more frequent (CoimbRA). Overall, 498 (31.4%) patients had no signs of inflammation as currently assessed, that is, they were in 3v remission (Table 1).

In the near-remission group ($n = 303$), the mean PGA was considerably above the ACR/EULAR Boolean cut-off of $\leqslant 1$ [mean 3.6 (S.D. 1.9)], with 70.3 and 43.9% of patients having a score >2 and >3, respectively (supplementary Fig. S1, available at *Rheumatology* Online).

Impact domains according to disease activity states

Table 2 presents disease impact domains according to remission status. In non-remission patients ($n = 1090$), all the disease impact domains had mean values >3.4, with coping, sleep and emotional well-being scoring lower/better than physical domains. Conversely, in remission patients ($n = 195$), only fatigue (mean 1.3) and physical well-being (mean 1.1) presented means >1.

Mean values of disease impact measures were very similar for patients in near-remission and in non-remission, except ($P < 0.05$) for the pain, physical well-being and function domains (Table 2). Mean scores of disease impact measures were markedly different between patients in remission and those in near-remission ($P < 0.001$ in all cases) (Table 2). These two groups are brought together under the concept of 3v remission, whose values of disease impact are, as expected, between the two (Table 2 and supplementary Table S1, available at *Rheumatology* Online).

Table 1 Demographic and clinical characteristics of 1588 RA patients

Characteristics	RAID (n = 348)	COMEDRA (n = 936)	CoimbRA (n = 304)	All patients (n = 1588)
Age[a], mean (S.D.), years	55.9 (12.9)	57.6 (11.1)	59.4 (12.4)	57.6 (11.8)
Female gender[a], n (%)	262 (75.9)	742 (79.3)	249 (81.9)	1253 (79.1)
Disease duration[a], mean (S.D.), years	12.7 (10.6)	13.5 (9.8)	11.9 (9.0)	13.0 (9.8)
Current biologic agents, n (%)	174 (50.0)	699 (74.7)	95 (31.3)	968 (61.0)
HAQ[a] (0–3), mean (S.D.)	1.18 (0.76)	0.40 (0.46)	1.09 (0.74)	0.70 (0.70)
TJC28 (0–28), mean (S.D.)	5.5 (6.5)	3.3 (4.2)	1.4 (2.9)	3.4 (4.8)
SJC28 (0–28), mean (S.D.)	3.7 (4.5)	2.2 (3.1)	1.4 (2.5)	2.4 (3.4)
CRP, mean (S.D.), mg/dl	1.1 (1.6)	0.5 (1.3)	0.8 (1.4)	0.7 (1.4)
PhGA[a] (0–10), mean (S.D.)	3.4 (2.4)	2.3 (1.7)	1.3 (1.5)	2.4 (2.0)
DAS28-ESR (4v)[a] (0–9.4), mean (S.D.)	4.0 (1.6)	3.1 (1.3)	2.8 (1.2)	3.2 (1.4)
Disease activity states, n (%)				
3v remission[b]	71 (20.4)	283 (30.2)	144 (47.4)	498 (31.4)
Remission[c]	21 (6.0)	146 (15.6)	28 (9.2)	195 (12.3)
Near-remission[d]	50 (14.4)	137 (14.6)	116 (38.2)	303 (19.1)
Non-remission	277 (79.6)	653 (69.8)	160 (52.6)	1090 (68.6)
PGA (0–10), mean (S.D.)	4.2 (2.5)	2.9 (2.1)	4.4 (2.7)	3.5 (2.4)
Pain (0–10), mean (S.D.)	4.7 (2.7)	3.0 (2.2)	4.9 (2.5)	3.7 (2.5)
Function (0–10), mean (S.D.)	4.5 (2.6)	2.8 (2.3)	4.9 (2.6)	3.6 (2.6)
Fatigue (0–10), mean (S.D.)	4.7 (2.7)	2.8 (2.7)	5.1 (2.7)	4.3 (2.8)
Sleep (0–10), mean (S.D.)	3.9 (3.0)	2.6 (2.7)	4.3 (2.8)	3.2 (2.9)
Physical well-being (0–10), mean (S.D.)	4.4 (2.5)	3.2 (2.3)	4.9 (2.4)	3.8 (2.5)
Emotional well-being (0–10), mean (S.D.)	3.7 (2.6)	2.8 (2.5)	4.6 (2.6)	3.4 (2.7)
Coping (0–10), mean (S.D.)	3.8 (2.5)	2.4 (2.3)	4.2 (2.6)	3.0 (2.5)
Full RAID score (0–10), mean (S.D.)	4.3 (2.2)	3.0 (2.0)	4.7 (2.3)	3.6 (2.3)

[a]Missing data for <10% of patients. [b]3v remission: TJC28, SJC28 and CRP (mg/dl) all $\leqslant 1$, but PGA not considered. It equates to merging the remission and near-remission disease states. [c]Remission: TJC28, SJC28, CRP (mg/dl) and PGA all $\leqslant 1$. [d]Near-remission: TJC28, SJC28 and CRP (mg/dl) all $\leqslant 1$ and PGA >1.

Table 2 Disease impact domains comparison according to disease activity states

Domains	Remission[a] (*n* = 195)		Near-remission[b] (*n* = 303)		Non-remission (*n* = 1090)		*P*-value	
	Mean (S.D.)	% ⩽1	Mean (S.D.)	% ⩽1	Mean (S.D.)	% ⩽1	Remission *vs* near-remission	Near-remission *vs* Non-remission
Fatigue	1.3 (1.9)	69	4.4 (2.4)	10	4.8 (2.7)	14	<0.001	0.050
Physical well-being	1.1 (1.5)	76	3.9 (2.0)	9	4.3 (2.4)	14	<0.001	0.012
Emotional well-being	1.0 (1.7)	80	3.6 (2.3)	22	3.7 (2.7)	24	<0.001	0.430
Sleep	1.0 (1.7)	80	3.5 (2.7)	28	3.6 (2.9)	31	<0.001	0.468
Pain	0.9 (1.2)	82	3.7 (2.1)	12	4.3 (2.4)	14	<0.001	<0.001
Function	0.8 (1.1)	81	3.6 (2.2)	14	4.1 (2.6)	17	<0.001	0.002
Coping	0.6 (1.2)	88	3.2 (2.3)	25	3.4 (2.5)	28	<0.001	0.324
RAID score	0.9 (1.0)	67	3.7 (1.9)	5	4.1 (2.2)	8	<0.001	0.008
PGA	0.5 (0.5)	100	3.6 (1.9)	0	4.0 (2.4)	15	<0.001	0.008

Domains in descending order by mean values in remission state. All domains are scored 0–10. *P*-values according to Student's *t*-test. [a]Remission: TJC28, SJC28, CRP (mg/dl) and PGA all ⩽1. [b]Near-remission: TJC28, SJC28 and CRP (mg/dl) all ⩽1 and PGA >1.

Drivers of PGA in near-remission patients

In the 303 near-remission patients, PGA presented moderate ($r_p = 0.47$, emotional well-being) to good ($r_p = 0.68$, pain) correlation with disease impact domains (all $P < 0.001$) (supplementary Table S2, available at *Rheumatology* Online). In multivariable analysis, PGA was explained ($R^2_{adjusted} = 0.55$) by pain ($\beta = 0.29$), function ($\beta = 0.23$), physical well-being ($\beta = 0.19$) and fatigue ($\beta = 0.15$).

Main drivers of differences of impact between disease activity states

Although both remission and near-remission patients had SJC28, TJC28 and CRP ⩽1, all mean values of impact domains were statistically higher in near-remission (supplementary Fig. S2, available at *Rheumatology* Online). Within these, physical and mixed domains of impact (pain, physical well-being, function and fatigue) presented greater ESs (~1.53) than psychological ones (still with a high ES >1.0). The same trend was found for comparisons between other disease activity groups, but with lower ESs (supplementary Fig. S2, available at *Rheumatology* Online). Global scores (PGA and RAID) were better discriminants than individual RAID domains only when comparing remission with near-remission patients (supplementary Fig. S2, available at *Rheumatology* Online).

Discussion

Several important findings emerged from this study exploring disease impact in different Boolean disease activity states. It was confirmed that ACR/EULAR Boolean-based remission is very stringent (12.3% of all patients). Near-remission, that is, failing to reach remission solely due to PGA, was at least as frequent as and up to four times more frequent than remission. Because of the influence of PGA, the percentage of patients classified as in remission was reduced from 31.4% (3v remission) to 12.3%. The scores of the diverse domains of impact in near-remission patients were similar to those for patients in non-remission and PGA was high in these patients (mean 3.6). Pain, physical well-being, function and fatigue were the impact domains that better differentiated remission from near-remission states. These results were confirmed by multivariable analyses, supporting the conclusion that high PGA in near-remission patients is driven by physical factors (which might represent subclinical inflammatory activity) and does not especially reflect psychological aspects, including anxiety or distress, or FM, contradicting common beliefs [7, 13].

This study has strengths and weaknesses. A weakness may be the relatively low percentage of patients in remission, which might limit the power. Using different multicultural cohorts imposes some cautions in the interpretation of results. However, it allowed for a larger sample and permitted us to analyse multicultural differences in PGA and its impact on the classification of remission. How PGA is measured and its relatively unclear cut-offs and formulations are another issue [7]. Using the same formulation in the three studies strengthened this pooled analysis. Some relevant comorbidities such as FM, depression and radiological damage were not assessed, although psychological distress and function were assessed through the RAID questionnaire [8]. Further studies might explore their influence on PGA. Finally, other measures of quality of life than the RAID would have strengthened this study.

One recent study explored PGA determinants in different levels of disease activity [14], but using tertiles of DAS28 instead of ACR/EULAR remission criteria [3] and the small sample rendered assessment of remission not feasible and a DAS28 <4.2 was adopted.

The ratio of near-remission *vs* remission rates was variable between studies, from 1:1 to 4:1. Possible reasons to explain this difference could include culture, which may affect PROs [15]. Other reasons could be differences in the provision of patient education, psychological support and patient expectations between countries. Near-remission rate differences could also be affected by the reliability of joint counts [16]. SJC and TJC may miss subclinical inflammation in joints [17], and totally ignore inflammation in other structures, such as tenosynovitis, which patients can still perceive and value. The use of US [18] or sensitive CRP measurement (which reflects inflammatory activity when routine CRP is $\leqslant 1$) [19] rather than current methods should be further explored, especially in patients in near-remission.

As expected, patients in remission had a low disease impact. Fatigue was, among this group of patients and also among all, the domain with the highest mean score, underlining its importance in the impact of RA, even in patients in remission [20].

The findings reported herein have important implications for clinical practice. Patients in near-remission presented high levels of symptoms, with mean scores $\sim$3.5. Although a higher cut-off for PGA in the definition of remission would certainly increase the number of remissions, it would not make clinical sense in patients whose high PGA is not related to residual inflammation but to structural damage or an unrelated comorbidity such as OA, depression or FM. Such patients would require adjunctive tailored interventions (e.g. patient education, physiotherapy, analgesics, antidepressants or cognitive behavioural therapy) and not the reinforcement of disease-modifying medication recommended to those not achieving remission. Another important issue is when to stop or taper immunosuppression—is the target then remission or near-remission? The present results support the idea that PGA poses problems when used in the combined definition of remission. Perhaps having two separate definitions of remission: one for the purposes of defining the target of immunosuppressive therapy (excluding PGA) and another that is patient based would make sense.

The impact of disease from the patient's perspective should continue to be taken very seriously, but this would be better served by an instrument that allows identification of the specific cause of persistent impact and thus guide adjunctive therapy. The RAID [8], taking its individual dimensions separately, may well be a good solution to this need.

Acknowledgments

We wish to thank Dr Mwidimi Ndosi (University of the West of England, Bristol, UK) for critically revising the manuscript for its intellectual content.

The CoimbRA Investigators, in addition to authors R.J.O.F., C.D. and J.A.P.d.S. are the following: Gisela Eugénio (Coimbra, Portugal) and Cristiana Silva (Coimbra, Portugal).

The RAID Investigators, in addition to authors L.G., M.d.W., M.D., J.R.K. and T.K.K. are the following: Andra Balanescu (Bucharest, Romania), Dimitrios T. Boumpas (Heraklion, Greece), Loreto Carmona (Madrid, Spain), Ben A. C. Dijkmans (Amsterdam, The Netherlands), Matthias Englbrecht (Erlangen, Germany), Feride Gogus (Ankara, Turkey), Turid Heiberg (Oslo, Norway), Emilio Martin Mola (Madrid, Spain), Marco Matucci Cerinic (Firenze, Italy), Kati Otsa (Tallinn, Estonia), Georg Schett (Erlangen, Germany) and Tuulikki Sokka (Jyväskylä, Finland).

The COMEDRA Investigators, in addition to authors M.D., M.S., L.G. and B.F. are the following: Françoise Fayet (Clermont-Ferrand, France), Mélanie Gilson (Grenoble, France), Alain Cantagrel (Toulouse, France), Sophie Pouplin (Rouen, France), René-Marc Flipo (Lille, France), Gael Mouterde (Montpellier, France), Liana Euller-Ziegler (Nice, France), Thierry Schaeverbeke (Bordeaux, France), Alain Saraux (Brest, France), Isabelle Chary-Valckenaere (Nancy, France), Gérard Chales (Rennes, France), Emmanuelle Dernis (Le Mans, France), Pascal Richette (Paris, France), Xavier Mariette (Le Kremlin-Bicetre, France), Francis Berenbaum (Paris, France) and Jean Sibilia (Strasbourg, France).

The RAID study was supported by the EULAR (grant number CLI.013). The COMEDRA trial (NCT01315652) was supported by a grant from the French National Research Program (grant number 2010-A 01 2996-33) and an unrestricted grant from Roche.

Funding: No specific funding was received from any bodies in the public, commercial or not-for-profit sectors to carry out the work described in this article.

Disclosure statement: The authors have declared no conflicts of interest.

Supplementary data

Supplementary data are available at *Rheumatology* Online.

References

1 Smolen JS, Landewe R, Bijlsma J *et al*. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. Ann Rheum Dis 2017 Published Online First: 2017/03/08. doi: 10.1136/annrheumdis-2016-210715.

2 Singh JA, Saag KG, Bridges SL *et al*. 2015 American College of rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Care Res 2016;68:1–25.

3 Felson DT, Smolen JS, Wells G *et al*. American College of Rheumatology/European League Against Rheumatism provisional definition of remission in rheumatoid arthritis for clinical trials. Arthritis Rheum 2011;63:573–86.

4 Studenic P, Smolen JS, Aletaha D. Near misses of ACR/EULAR criteria for remission: effects of patient global

assessment in Boolean and index-based definitions. Ann Rheum Dis 2012;71:1702–5.

5 Vermeer M, Kuper HH, van der Bijl AE *et al*. The provisional ACR/EULAR definition of remission in RA: a comment on the patient global assessment criterion. Rheumatology 2012;51:1076–80.

6 Balogh E, Dias JM, Orr C *et al*. Comparison of remission criteria in a tumour necrosis factor inhibitor treated rheumatoid arthritis longitudinal cohort: patient global health is a confounder. Arthritis Res Ther 2013;15:R221.

7 Nikiphorou E, Radner H, Chatzidionysiou K *et al*. Patient global assessment in measuring disease activity in rheumatoid arthritis: a review of the literature. Arthritis Res Ther 2016;18:251.

8 Gossec L, Paternotte S, Aanerud GJ *et al*. Finalisation and validation of the rheumatoid arthritis impact of disease score, a patient-derived composite measure of impact of rheumatoid arthritis: a EULAR initiative. Ann Rheum Dis 2011;70:935–42.

9 Dougados M, Soubrier M, Perrodeau E *et al*. Impact of a nurse-led programme on comorbidity management and impact of a patient self-assessment of disease activity on the management of rheumatoid arthritis: results of a prospective, multicentre, randomised, controlled trial (COMEDRA). Ann Rheum Dis 2015;74:1725–33.

10 Ferreira RJO, Duarte C, Ndosi M *et al*. Suppressing inflammation in rheumatoid arthritis: Does patient global assessment blur the target? A practice–based call for a paradigm change. Arthritis Care Res 2017; doi: 10.1002/acr.23284. (in press).

11 Svensson B, Andersson ML, Bala SV, Forslind K, Hafstrom I. Long-term sustained remission in a cohort study of patients with rheumatoid arthritis: choice of remission criteria. BMJ Open 2013;3:e003554.

12 Tälli S, Etcheto A, Fautrel B *et al*. Patient global assessment in psoriatic arthritis – what does it mean? An analysis of 223 patients from the psoriatic arthritis impact of disease (PsAID) study. Joint Bone Spine 2016;83:335–40.

13 Coury F, Rossat A, Tebib A *et al*. Rheumatoid arthritis and fibromyalgia: a frequent unrelated association complicating disease management. J Rheumatol 2009;36:58–62.

14 Ward MM, Guthrie LC, Dasgupta A. Direct and indirect determinants of the patient global assessment in rheumatoid arthritis: Differences by level of disease activity. Arthritis Care Res 2017;69:323–9.

15 Putrik P, Ramiro S, Hifinger M *et al*. In wealthier countries, patients perceive worse impact of the disease although they have lower objectively assessed disease activity: results from the cross-sectional COMORA study. Ann Rheum Dis 2015;75:715–20.

16 Cheung PP, Gossec L, Mak A, March L. Reliability of joint count assessment in rheumatoid arthritis: a systematic literature review. Semin Arthritis Rheum 2014;43:721–9.

17 Saleem B, Brown AK, Keen H *et al*. Should imaging be a component of rheumatoid arthritis remission criteria? A comparison between traditional and modified composite remission scores and imaging assessments. Ann Rheum Dis 2011;70:792–8.

18 Horton SC, Tan AL, Freeston JE *et al*. Discordance between the predictors of clinical and imaging remission in patients with early rheumatoid arthritis in clinical practice: implications for the use of ultrasound within a treatment-to-target strategy. Rheumatology 2016;55:1177–87.

19 Dessein PH, Joffe BI, Stanwix AE. High sensitivity C-reactive protein as a disease activity marker in rheumatoid arthritis. J Rheumatol 2004;31:1095–7.

20 Druce KL, Bhattacharya Y, Jones GT, Macfarlane GJ, Basu N. Most patients who reach disease remission following anti-TNF therapy continue to report fatigue: results from the British Society for Rheumatology Biologics Register for Rheumatoid Arthritis. Rheumatology 2016;55:1786–90.