Title: “It can't be zero!” - Difficulties in completing patient global assessment in rheumatoid arthritis: a mixed methods study.

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Word count: 3743

Acknowledgments

We wish to thank to all participants who accepted our invitation to participate in this study. We also wish to thank Professor Laure Gossec (UPMC University Paris 06, Paris, France) for her contribution in the design of this study and helpful comments in the early manuscripts drafts.

Conflict of interests

The authors have declared no conflicts of interest.

Funding

This study received no funding.

ABSTRACT

Objectives: Patient global assessment (PGA) is purported to add patient's perspective in the composite measures of rheumatoid arthritis (RA). However, PGA is not standardized and it is unknown whether patient's interpretation of the measure is consistent with its intended purpose. This study aimed to explore difficulties experienced by patients with RA in completing PGA, and assess the impact of a structured explanation in improving its validity and reliability.

Methods: Mixed methods study, using interviews, focus groups and PGA data. During interviews, patients (convenience sample, n=33) completed three often used PGA formulations. Then a nurse provided structured explanation about what PGA is and why it is used. After further discussion, patients completed one PGA version again. Interviews were recorded, transcribed and analysed using inductive thematic analysis. We compared PGA scores pre- and post-explanation (Wilcoxon Signed-Ranks) and the proportion of patients achieving RA remission with PGA≤1 (McNemar's tests).

Results: Three themes emerged: understanding the meaning of PGA, the purpose of PGA and measurement difficulties. The difficulties caused systematic errors in PGA completion such as marking higher when feeling well, marking near the centre or away from zero. The structured explanation was helpful.

Following the explanation, the median PGA score decreased from 3.0 to 2.1cm; and the proportion of non-remission solely due to PGA>1 from 52% to 41%; none of these changes were statistically significant.

Conclusions: Many patients have difficulties in completing PGA. Standardisation of PGA and a structured explanation may improve its clarity, validity and reliability.

Keywords: Nursing, Mixed method study, Patient education, Outcome assessment, Patient reported outcome measures, Remission, Rheumatoid Arthritis.

KEY MESSAGES

- Many patients with rheumatoid arthritis (RA) are unaware of the patient global assessment (PGA)'s purpose
- Patients have difficulties in completing the PGA reliably, thus undermining the validity of the measure
- A standardized formulation and a structured explanation to the patient may improve the PGA validity

INTRODUCTION

The patient global assessment (PGA) is a self-report measure widely used in rheumatology [1] and in other long-term conditions such as neurology [2], cardiology [3], psychiatry [4], dermatology [5], and gastroenterology [6]. The PGA is meant to generally reflect patient's own assessment of severity of the condition and is included in disease activity indices used to guide therapy decisions.

It is hard to identify when and how PGA was developed but initially it was designated as "global health", with earliest references in PubMed dated 1977 [7], and 1980 with the studies on the "Arthritis Impact Measurement Scales" [8]. The use of PGA was boosted in the early nineties, by its inclusion in the widely implemented "Disease Activity Score" (DAS) [9, 10] and in the American College of Rheumatology (ACR) core set of disease activity measures for RA clinical trials [11]. The incorporation of PGA in these composite measures was justified, mainly, by its high sensitivity to change, as documented in meta-analyses [12] or in other comparative studies [13]. PGA is also practical and easy to administer, it has good face validity and test-retest reliability. It provides additional information to the clinician (patient perspectives of disease activity).[1] These strengths have made PGA the second most used patient reported outcome in RA clinical trials next to the health assessment questionnaire (HAQ) [14, 15]. In 2011, the ACR and the European League Against Rheumatism (EULAR) defined the criteria for RA remission, which attributed to PGA the same weight as that of tender and swollen joint counts (TJC28, SJC28) and inflammatory markers (c-reactive protein - CRP); all required to be ≤ 1 [16]. This reflects the growing significance of the patient's perspective because the current pharmacological management of RA resides in treating to target, the target being remission [17, 18].

Incorporating the PGA in composite indices did not happen without controversy. Its validity and reliability have been questioned [19-22]. There are many versions of PGA, which ask about different concepts ('Considering all the ways the *disease* affects you…', 'Considering all the ways your *arthritis* has affected you…' 'How well do you consider your *health state* …' 'How active

was your *arthritis*…'); different time references (today, past week) and different anchor descriptors ('Doesn't affect - Affect a lot', 'Very well - Very poor', 'The best - The worst') [1, 23]. One of the main concerns is the interchangeable use of different PGA formulations, and this has been shown to influence the remission rate up to 6.3% among disease activity indices [23]. A recent systematic review [1] indicates that many studies still test the properties and concepts underlying PGA. Recent research has shown that PGA is predominantly related to disease impact domains (pain, fatigue, functional disability and psychological distress) rather than to disease activity itself (inflammatory markers) [24], thus questioning the validity of incorporating PGA in RA remission definitions [23-25]. This led to a proposal to remove PGA from the RA remission definition, which has also been controversial [26, 27]. Understanding what patients consider when they answer the PGA question may help shed light in this on-going debate.

The aims of this study were to explore patients' difficulties in completing PGA, and to explore the impact of a structured explanation about PGA, with the purpose of improving its validity and reliability.

METHODS

Design

This was a mixed methods study with a "qualitative dominant" component [28]. Qualitative and quantitative data were concurrently collected and analysed separately before integration in the interpretation phase [29]. Qualitative data were obtained by semi-structured individual interviews and focus groups (FG). Quantitative data were obtained from participants' responses to three different formulations of PGA (See "data collection" bellow), used to facilitate discussions, one of which was repeated after a structured explanation (see "intervention" below).

Participants

Consecutive sampling was used to recruit adult patients satisfying current RA criteria [30,

31] via one rheumatology clinic centre in a large university hospital in the centre of Portugal. Patients were excluded if they were unable to read and answer the questionnaires unaided.

Intervention

The intervention consisted of a brief (<5 minutes) structured explanation on (i) what is expected to be captured by PGA, i.e. what patient feels is affecting his/her well-being as a consequence of the RA, or in other words, caused/triggered by active "inflammation", such as swelling in joints, pain, stiffness, fatigue, that is not likely caused by other medical conditions (examples were provided), (ii) how PGA is included in disease activity indices (DAS28 and Simplified Disease Activity Index (SDAI)), and (iii) how these composite indices are used to guide treatment decisions. The structured explanation was first pre-tested with 3 participants, leading to simplification in the wording. The first author (RF, registered nurse) delivered the intervention using visual aids (See Supplementary Figures S1A to S1H).

Data Collection

Data collection was performed between November 2016 and January 2017. An interview guide (See Supplementary Table S1) was developed by the research team, pilot-tested with three patients not included in the sample, and used in both individual interviews and FGs.

First, participants completed a form with their demographic and clinical data and they were requested to complete one formulation of PGA to prompt discussion. Two additional versions of PGA were applied, one at a time. The three formulations were selected for their variances in concept and time frame under evaluation, all using a visual analogue scale (VAS, 0-100mm): Version 1 - “Considering all the ways the disease affects you, how did you feel over the last week?”[8] (anchors: "Doesn't affect" - "Affect a lot"), Version 2 - "Considering all of the ways your arthritis has affected you, how do you feel your arthritis is today?"[16] ("Very well" - "Very poor"), and Version 3 - "How would you assess your health state during the past week?"[9, 10] ("The best"

- "The worst"). For each version, participants were asked to carefully read the question, mark their answer and then to reflect in silence and write down their thoughts and keywords. Following the discussion of the three formulations, the intervention was given and participants were asked to discuss again. Finally, the participants were asked to re-assess version 2 of PGA, as this is the most accepted [1, 16].

An experienced and trained qualitative researcher and interviewer (RF) led the discussion. All interviews took place in a quiet room in the rheumatology department. The interviews took approximately 35-40 minutes and were audio taped and anonymised (P1 to P33) at transcription, completed with field notes.

The disease activity on the day of the interview was derived from clinical records in order to assess the influence of PGA on the remission status. The ACR/EULAR Boolean-based definition of remission [16] and the following categories were used: (i) remission: SJC28, TJC28, CRP in mg/dl, and PGA all ≤1, (ii) PGA-near-remission: only PGA is >1, and (iii) non-remission: SJC28, TJC28, or CRP in mg/dl are >1 [24].

Ethical considerations

The study adhered to Good Clinical Practice in research and the Ethics Committee of the Centro Hospitalar e Universitário de Coimbra, Portugal, approved the study (CHUC-093-16). Participants provided a written informed consent before study procedures started.

Data analysis

Inductive thematic analysis [32, 33] was used to ensure that qualitative findings were grounded in patients' data. Transcripts were made a few days after interviews and were read and reread by the first author to gain an understanding of, and familiarisation with the issues and patterns. Then, small units of meaning were identified line-by-line and given descriptive labels (codes). Next, the findings were explored to see how codes could be grouped to form categories

and/or overarching themes. Data management and analysis were facilitated by ATLAS.ti v.1.0.51 software.

For analysis of the quantitative data we used: (i) Wilcoxon Signed-Ranks Test to compare PGA scores before and after the intervention, and (ii) McNemar's test to compare the proportion of PGA-Near-remission patients before and after the intervention. IBM® SPSS® Statistics, version 20.0 software was used.

Validity and reliability/Rigour

The qualitative data analysis was carried out independently by two researchers (RF and MH), who later discussed and subsequently agreed on codes and themes. The resulting categorization and data interpretation was discussed and improved with the wider research team, which included three nurses, three patient research partners, two rheumatologists, and one medical student. The resulting themes were presented to 10 of the 33 participants for validation of the data interpretation made by the researchers.

RESULTS

Patient characteristics

Forty patients were invited to the study but seven declined participation. Of the 33 participants , 7 were interviewed individually and 26 took part in 8 FGs. Participants' age range was 42 to 82 years, disease duration 1 to 48 years and 76% were women. Table 1 presents participants' characteristics.

Qualitative findings: Difficulties experienced by patients in completing PGA

Three overarching themes emerged from the qualitative data analysis: i) understanding the meaning of PGA, ii) measurement difficulties, and iii) understanding the purpose of PGA. The categorisation is visualised in Figure 1 and themes are presented below, supported by quotes.

Additional quotes are presented in Tables 2-4.

i) Understanding the meaning of PGA

When discussing what participants thought about or considered when completing the PGA, pain was clearly the most mentioned symptom. Pain limited their daily activities, such as self-care, walking, climbing stairs, work and participation activities (Table 2).

Other symptoms that participants associated with PGA were fatigue, limitations in leisure activities, stiffness or psychological distress. Regarding fatigue, the participants did not know whether or not it was associated with RA, but they found it affecting many aspects of life such as work, self-care, walking, thinking or even talking. The psychological distress encompassed a spectrum of disease-related anxieties, from fears that arose with the diagnosis or with blood tests to suicide ideation (Table 2).

> "The pain upsets me, the tiredness, the fact that I can't do my life, I thought I was going to be disabled. I think about suicide" (P31)

Participants also considered how some comorbidities and RA sequelae affected their PGA score. One example given was how difficult it was to ascertain the origin of pain, although PGA requires only the pain/discomfort caused by RA to be considered:

> "(...) we always have to think about the joints, the joints and not the spine, for example, an herniated disc (…). Because when we read this we need to see «it's only arthritis». So, I have to try to distinguish and sometimes we don't even think about it." (P5)

The meaning of PGA was also complicated by the use of different PGA formulations, namely by the terminology arthritis *vs* disease *vs* health. Although for some patients the three words are similar: "To me, there's no difference" - (P10), most participants considered them to address different concepts. It was also mentioned that this might be particularly difficult for people affected

by depression.

> "Health involves my head too. It's not only arthritis for sure." (P7)
>
> "The disease is everything in general, right? Not just the arthritis itself. The arthritis is the arthritis! The health one is everything again, right?" (P8)

ii) Measurement difficulties

Several measurement issues emerged from the interviews and these are presented in two sub-themes: scaling difficulties and time reference difficulties (Table 3).

Scaling difficulties

At least three participants completed the VAS without paying attention to the anchor descriptors, assuming that 10cm (or 100mm) is good (similar to "feeling 100%"). Others felt confused by the anchors after completing several questionnaires, some with similar questions but opposite anchors. The question as to whether 100 is good or bad was often raised. Some participants expressed difficulties with the scaling conversion, questioning whether 0-10 was the same as 0-100. The presentation of PGA through numeric rating scale (NRS) vs VAS also causes difficulties of interpretation for some patients (Table 3).

> "I always put 100 which is good (...). There are other [scales] where zero is good and 100 isn't, it depends on how they put it. In this case right here I think 100 is the good one" (P2)

The subjective nature of the concept being assessed (PGA) was also pointed out as a difficulty because the quantification of a feeling or sensation or impact of disease is very different from individual to individual:

> "It also depends from person to person, there are some more mushy… (…) It has happened to me: [the doctor says] «oh, you don't have complaints? You have everything inflamed. You're very tough.»" (P3)

Scoring in the extremes, especially the minimum was very rare and some participants clearly stated: 'It can't be zero'. Different reasons given were: (i) the fear that scoring the PGA near to zero could lead to the withdrawal of medications, especially the expensive bDMARDS; (ii) the presence of comorbidities and RA sequelae (e.g. thumb osteoarthritis) that will never allow the patient to be in a perfect health status; (iii) patients want to take into account the fluctuation nature of RA disease activity. Therefore, some participants felt the need to refrain from considering a score of 0 or nearing to it even when they had no active disease.

> "I can never answer 0, because I always have something that affects me. Someday I feel nothing, it goes well, but on other days the pain comes back from nowhere." (P29)

Time reference difficulties

Different PGA formulations refer to different time reference - over the last week (version 1 & version 3) and today (version 2). This raised assessment problems and for most participants it was easier answering about today than trying to "average" the last week, which can be subject to a recall bias.

> "[Today] is different from the week (…) it's definitely easier. When they ask a week, we have to go back in time and the pain isn't the same anymore. (...) And today, it is easy to remember." (P5)

Naturally, patients express that assessing only one day ("Today") instead of a week is less representative of the disease burden, and more often lower, which depends if the symptoms fluctuated or not.

It also seems that when asked about "today" patients are more likely to recall all their disease history as reference, or in other words, they seem to interpret "Today" as "Nowadays" in opposition as the time of the disease onset.

> “«last week» is what happened last week and the other one [PGA2 - "today"] is since I was diagnosed with RA.” (P12)

iii) Understanding the purpose of PGA

None of the participants had knowledge about how the PGA score is integrated in composite disease activity indices such as DAS28 and how this would affect the selection or adjustment of their treatment. Only a few participants mentioned the PGA would serve to adjust the treatment, but most of them had the feeling the PGA is 'not used to adjust the treatment', but rather used to assess patient psychological well-being, disease evolution or to identify any complication that might preclude bDMARD administration (Table 4).

> "I thought it [the PGA] was only meant to check on how we were feeling (...) for psychological evaluation (...) That it had no influence…"(P10)

Some participants also expressed the view that 'only the Doctor's judgment counts', meaning that they were asked of PGA only to confirm the rheumatologist's opinion, which is based on objective measures of disease. PGA would not be considered if it contradicts doctor's perceptions, that is: the doctor had already made his decision.

> “It will [influence the treatment] if the answer is somehow according to the blood tests we make. If it doesn’t agree, maybe it’s not important.” (P3)
>
> “Honestly? I think the doctor sometimes asks that only as a routine – he doesn’t really value it (…)”(P5)

Other participants considered that PGA is used 'for research only', namely to evaluate the efficacy of new treatments.

After the intervention individually patients confirmed the 'value of a structured explanation', suggesting that this information was new to them and that it would influence their subsequent

assessments:

> "Sometimes I just give a random number (…) now maybe I will think more carefully and try to be as accurate as possible" (P4).

Quantitative results

Pre- vs post intervention differences on PGA score and on remission classification

After the structured explanation, 15 (51.7%) participants decreased their PGA scores, while 9 (31.0%) increased them, and 5 (17.3%) gave exactly the same score given before the intervention (Table 5). The median (Interquartile range) PGA scores before and after the intervention were 3.0 (1.4 to 6.9) cm and 2.1 (1.0 to 5.9) cm respectively. These differences were not statistically significant (Z=104, p=0.188).

Before the intervention, only 5 patients (17.3%) satisfied the ACR/EULAR Boolean-based remission criteria but after the intervention 8 patients (27.6%) attained this state. The proportion of patients failing Boolean-based remission solely because of a PGA>1 was 52% pre-intervention and 41% post-intervention (Table 5), a difference that was not statistically significant (p=0.375).

DISCUSSION

This study has shown that an instrument widely used in rheumatology, the PGA, has considerable assessment and interpretation issues. This mixed-methods approach allows a better understanding of several difficulties experienced by patients with RA when completing this measure. The overall results suggest that we cannot be sure whether the PGA provides a valid representation of what it is intended to measure and that there is a need for a standardized version. This study has increased our understanding of the impact of the interchangeable (unstandardized) use of different formulations of PGA on the scores given by patients. These are likely to have consequences on disease activity assessment and may affect subsequent treatment decisions. This was also the first study to explore the effect of a relatively simple and brief intervention (a

structured explanation about PGA, given by a nurse) on the scores of PGA and the proportion of patients attaining remission.

The qualitative analysis resulted in three themes explaining the difficulties in completing the PGA. First, participants had difficulties in understanding the meaning of PGA. The vast majority of the participants identified pain as the main factor that was associated with disease activity, followed by function, fatigue, psychological well-being, and other symptoms. They found it hard to exclude from consideration both comorbidities and sequelae of RA. These results are in accordance with previous quantitative and qualitative research [34-39]. The influence of contextual factors (not directly related to RA inflammation) upon PGA, such as psychological distress, coping and comorbidities, is also well documented [1, 24, 38-40].

Second, there were difficulties related to the measurement of PGA. Different measurement scales such as the use of entire numbers (NRS) or a continuous line to select one specific point (VAS), have been shown to require different levels of conceptualisation from the patient, with the first being easier to understand and mark. Some patients frequently assume that the anchors are always the same and many spontaneously adopt the right side or the higher number, especially 100 (“100%”), as meaning a better status. This issue has also been identified in other instruments [41] and diseases [42]. This may be explained to some extent, by the principles of Gutenberg Diagram, which describes the visual hierarchy and mind motion variations according to cultures and the direction of the reading [43]. There are also studies showing that right-handers’ tend to associate “good” with “right” and “bad” with “left” sides [44].

Participants identified important meaning differences between the diverse PGA formulations, that might affect subsequent assessment, and some seem to prefer the formulation that asks for "arthritis" and about "today", mainly because it is easier. This is not surprising given the shortest time period recall. However, this may be a major shortcoming of this PGA version. Patients come to see a health professional once every 3 to 6 months and ideally, it would be better to have an

instrument that captures what is going on in a patient over a longer period, including crises such as RA flares.

Some participants, unaware of the purpose and use of PGA, gave a random number in the middle of the scale to avoid being near to zero. Some participants expressed doing this for fear of having their medication decreased. This observation supports previous findings that some patients, despite feeling an absence or reduction of symptoms and a "sensation of return to normality", for strategic reasons, rarely use this end of the scale [45, 46].

Finally, participants were unaware how their PGA would inform the composite disease activity indices and thus influence treatment decisions. Providing a structured instruction on the purpose of PGA may help patients see its importance and give it more thought before completing the measure, thus increasing its validity. Patients may also benefit from more education on how nurses and physicians use patient-reported disease measures [34, 47].

The change in the median PGA score and the remission rate after the intervention was not statistically significant. However, an 11% increase in the proportion of patients attaining near-remission (from 41% to 52%) immediately after the intervention suggests that this deserves attention and warrants a further investigation.

This investigation has some limitations. First, cultural and educational factors, inherent to a single centre study can limit its generalisability. However, the results are generally in agreement with those of a recent report involving 300 patients with RA from the USA, 40% of which found PGA confusing, and emphasizing the relevance of lower health literacy and depressive symptoms in this confusion [47]. Second, as the youngest participant was 42 years old, this study does not embody the PGA understandings of younger people with RA. Third, a relative small sample was enrolled, and last, the effect of the structured explanation was tested on only one PGA formulation. Major strengths of this study were the use of three PGA formulations and the inclusion of patients with different disease activity states and not only patients who had an overall assessment divergent

from the rheumatologist. Another strength is the use of mixed-methods design and the involvement of three patient research partners.

In conclusion, this study found that patients have difficulties in understanding the meaning and the purpose of PGA. The tool had measurement difficulties arising from interpretation issues. The use of different versions of PGA as equivalent is problematic and can lead to different biases in the assessment of disease impact. Our study has shown that a structured explanation about PGA, given by a nurse and including its intended meaning and purpose, may help patients to complete this measure in a more meaningful way, thus likely to improve the validity of the assessment. This intervention has been shown to be feasible and further studies should test its effect using an adequately powered sample, multicentre and longitudinal design.

References:

1. 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.

2. Herring WJ, Snyder E, Tao P, Svetnik V, Lines C. Performance of the Patient Global Impressions – Severity Scale as a Self-reported Patient Assessment of Insomnia Severity (P1.107). Neurology 2018;90.

3. Cooper TJ, Anker SD, Comin-Colet J, et al. Relation of Longitudinal Changes in Quality of Life Assessments to Changes in Functional Capacity in Patients With Heart Failure With and Without Anemia. Am J Cardiol 2016;117:1482-7.

4. Lam RW, Lamy FX, Danchenko N, et al. Psychometric validation of the Perceived Deficits Questionnaire-Depression (PDQ-D) instrument in US and UK respondents with major depressive disorder. Neuropsychiatric disease and treatment 2018;14:2861-77.

5. Pascoe VL, Enamandram M, Corey KC, et al. Using the physician global assessment in a clinical setting to measure and track patient outcomes. JAMA dermatology 2015;151:375-81.

6. Adam B, Liebregts T, Saadat-Gilani K, Vinson B, Holtmann G. Validation of the gastrointestinal symptom score for the assessment of symptoms in patients with functional dyspepsia. Aliment Pharmacol Ther 2005;22:357-63.

7. Calabro JJ, Andelman SY, Caldwell JR, et al. A multicenter trial of sulindac in osteoarthritis of the hip. Clin Pharmacol Ther 1977;22:358-63.

8. Meenan RF, Gertman PM, Mason JH. Measuring health status in arthritis. The arthritis impact measurement scales. Arthritis Rheum 1980;23:146-52.

9. van der Heijde DM, van 't Hof MA, van Riel PL, et al. Judging disease activity in clinical practice in rheumatoid arthritis: first step in the development of a disease activity score. Ann Rheum Dis 1990;49:916-20.

10. van der Heijde DM, van't Hof MA, van Riel PL, et al. Validity of single variables and composite indices for measuring disease activity in rheumatoid arthritis. Ann Rheum Dis 1992;51:177-81.

11. Felson DT, Anderson JJ, Boers M, et al. The American College of Rheumatology preliminary core set of disease activity measures for rheumatoid arthritis clinical trials. The Committee on Outcome Measures in Rheumatoid Arthritis Clinical Trials. Arthritis Rheum 1993;36:729-40.

12. Gotzsche PC. Sensitivity of effect variables in rheumatoid arthritis: a meta-analysis of 130 placebo controlled NSAID trials. J Clin Epidemiol 1990;43:1313-8.

13. Bombardier C, Raboud J. A comparison of health-related quality-of-life measures for rheumatoid arthritis research. The Auranofin Cooperating Group. Control Clin Trials 1991;12:243s-56s.

14. Kilic L, Erden A, Bingham CO, 3rd, Gossec L, Kalyoncu U. The Reporting of Patient-reported Outcomes in Studies of Patients with Rheumatoid Arthritis: A Systematic Review of 250 Articles. J Rheumatol 2016;43:1300-5.

15. Kalyoncu U, Dougados M, Daures JP, Gossec L. Reporting of patient-reported outcomes in recent trials in rheumatoid arthritis: a systematic literature review. Ann Rheum Dis 2009;68:183-90.

16. 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. Ann Rheum Dis 2011;70:404-13.

17. Smolen JS, Landewé R, Bijlsma J, et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2016 update. 2017;76:960-77.

18. Smolen JS, Breedveld FC, Burmester GR, et al. Treating rheumatoid arthritis to target: 2014 update of the recommendations of an international task force. 2016;75:3-15.

19. van Tuyl LH, Boers M. Patient's global assessment of disease activity: what are we measuring? Arthritis Rheum 2012;64:2811-3.

20. 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 (Oxford) 2012;51:1076-80.

21. 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.

22. Masri KR, Shaver TS, Shahouri SH, et al. Validity and reliability problems with patient global as a component of the ACR/EULAR remission criteria as used in clinical practice. J Rheumatol 2012;39:1139-45.

23. Ferreira RJO, Eugenio G, Ndosi M, et al. Influence of the different "patient global assessment" formulations on disease activity score by different indices in rheumatoid arthritis. Clin Rheumatol 2018;37:1963-9.

24. 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 (Hoboken) 2018;70:369-78.

25. Ferreira RJO, Dougados M, Kirwan J, et al. Drivers of patient global assessment in patients with rheumatoid arthritis who are close to remission: an analysis of 1588 patients. Rheumatology (Oxford) 2017;56:1573-8.

26. Ferreira RJO, Duarte C, Ndosi M, et al. The controversy of using PGA to define remission in RA. Nat Rev Rheumatol 2018;14:245.

27. van Tuyl LHD, Boers M. Rheumatoid arthritis: Remission - keeping the patient experience front and centre. Nat Rev Rheumatol 2017;13:573-4.

28. Johnson RB, Onwuegbuzie AJ, Turner LA. Toward a Definition of Mixed Methods Research. Journal of Mixed Methods Research 2007;1:112-33.

29. Zhang W, Creswell J. The use of "mixing" procedure of mixed methods in health services research. Med Care 2013;51:e51-7.

30. Arnett FC, Edworthy SM, Bloch DA, et al. The American Rheumatism Association 1987 revised criteria for the classification of rheumatoid arthritis. Arthritis Rheum 1988;31:315-24.

31. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2010;69:1580-8.

32. Thorne S, Kirkham SR, MacDonald-Emes J. Interpretive description: a noncategorical qualitative alternative for developing nursing knowledge. Res Nurs Health 1997;20:169-77.

33. Thorne S, Kirkham SR, O'Flynn-Magee K. The Analytic Challenge in Interpretive Description. International Journal of Qualitative Methods 2004;3:1-21.

34. Studenic P, Radner H, Smolen JS, Aletaha D. Discrepancies between patients and physicians in their perceptions of rheumatoid arthritis disease activity. Arthritis Rheum 2012;64:2814-23.

35. Gossec L, Dougados M, Rincheval N, et al. Elaboration of the preliminary Rheumatoid Arthritis Impact of Disease (RAID) score: a EULAR initiative. Ann Rheum Dis 2009;68:1680-5.

36. 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 & Research (Hoboken) 2017;69:323-9.

37. van Tuyl LH, Sadlonova M, Hewlett S, et al. The patient perspective on absence of disease activity in rheumatoid arthritis: a survey to identify key domains of patient-perceived remission. Ann Rheum Dis 2017;76:855-61.

38. Walter MJ, Van't Spijker A, Pasma A, Hazes JM, Luime JJ. Focus group interviews reveal reasons for differences in the perception of disease activity in rheumatoid arthritis. Qual Life Res 2017;26:291-8.

39. Kvrgic Z, Asiedu GB, Crowson CS, Ridgeway JL, Davis JM, 3rd. "Like No One Is Listening to Me": A Qualitative Study of Patient-Provider Discordance Between Global Assessments of Disease Activity in Rheumatoid Arthritis. Arthritis Care Res (Hoboken) 2018;70:1439-47.

40. Challa DNV, Crowson CS, Davis JM, 3rd. The Patient Global Assessment of Disease Activity in Rheumatoid Arthritis: Identification of Underlying Latent Factors. Rheumatology and therapy 2017;4:201-8.

41. Ferreira RJO, Gossec L, Duarte C, et al. The Portuguese Rheumatoid Arthritis Impact of Disease (RAID) score and its measurement equivalence in three countries: validation study using Rasch Models. Qual Life Res 2018;27:2909-21.

42. Van Tubergen A, Debats I, Ryser L, et al. Use of a numerical rating scale as an answer modality in ankylosing spondylitis-specific questionnaires. Arthritis Rheum 2002;47:242-8.

43. Eldesouky DFB. Visual hierarchy and mind motion in advertising design. Journal of Arts and Humanities 2013;2:148-62.

44. Casasanto D, Chrysikou EG. When left is "right". Motor fluency shapes abstract concepts. Psychol Sci 2011;22:419-22.

45. van Tuyl LH, Hewlett S, Sadlonova M, et al. The patient perspective on remission in rheumatoid arthritis: 'You've got limits, but you're back to being you again'. Ann Rheum Dis 2015;74:1004-10.

46. Inanc N, Yilmaz-Oner S, Can M, Sokka T, Direskeneli H. The role of depression, anxiety, fatigue, and fibromyalgia on the evaluation of the remission status in patients with rheumatoid arthritis. J Rheumatol 2014;41:1755-60.

47. Hirsh J, Wood P, Keniston A, et al. Limited health literacy predicts patient confusion about patient global assessments of disease activity and rheumatoid arthritis model disease states. Arthritis Care Res (Hoboken) 2018 Published Online First: 2018/06/29. doi: 10.1002/acr.23692.

Table 1. Participant's characteristics (n=33)

Variable	N (%)
Gender (Female)	25 (76)
Age, years	
42-52	6 (18)
53-62	12 (36)
63-72	12 (36)
73-82	3 (9)
Education background, years	
≤4	15 (46)
5-9	10 (30)
10-12	6 (18)
>12	2 (6)
Disease duration, years	
1-5	8 (24)
6-10	4 (12)
>10	21 (64)
Treated with bDAMRDS, Yes	12 (36)

bDMARD, disease modifying anti-rheumatic drugs

Figure 1 – Overarching themes and codes of participant's difficulties in completing patient global assessment (PGA)

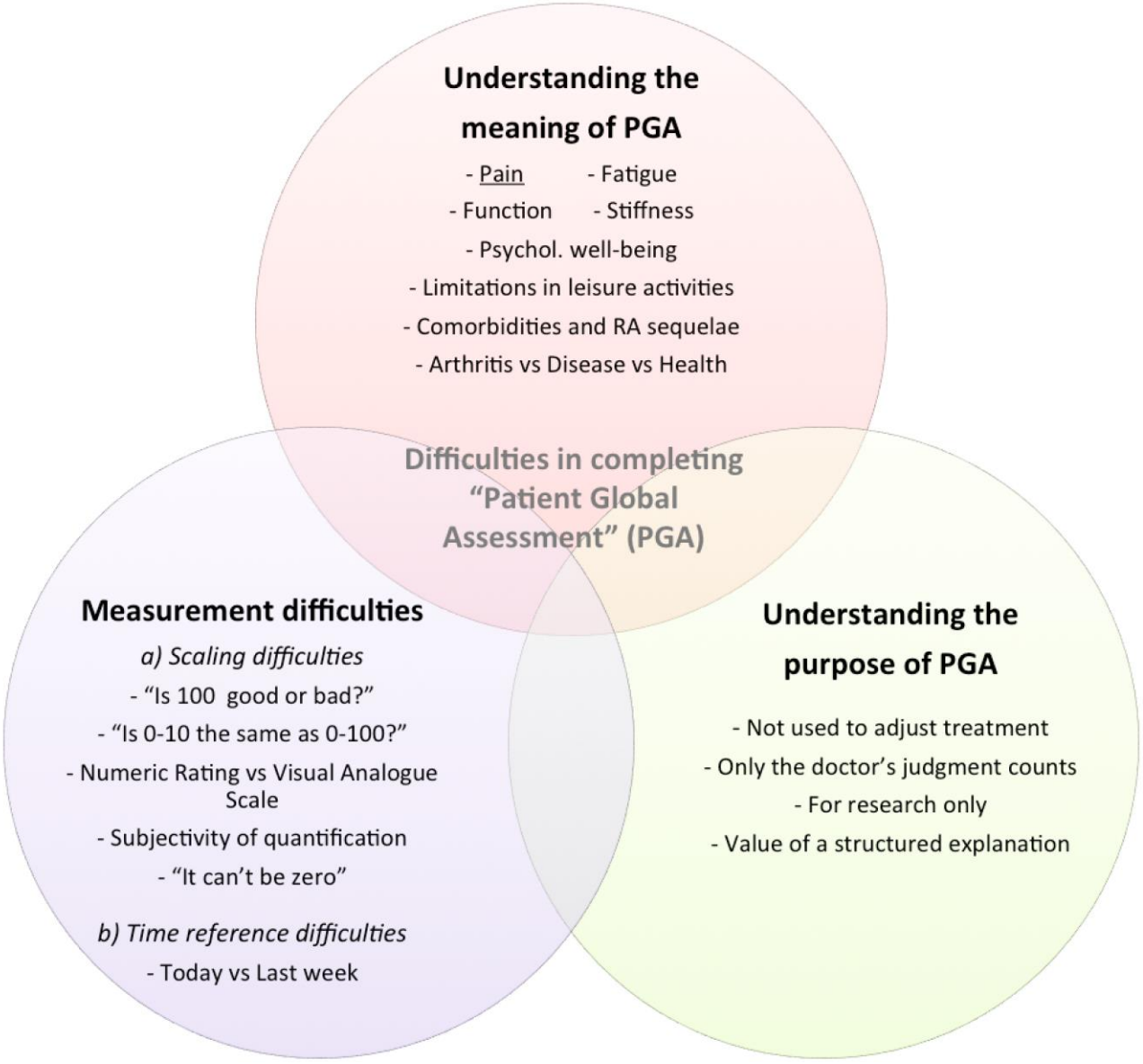

Table 2. Quotes supporting the theme "Understanding the Meaning of PGA" and its different codes

Codes	Quotes (Participant)
Pain	"I think about pain because that's what worries me the most" (P9, F, 66y, PGA=4.5, Non-Remission) "Yes, I thought about the pain in my hand (...) Everyday it hurts in a different site." (P20, F, 71y, PGA=1.9, Near-remission) "(…) I can't work with so much pain (…) I want to do my daily activities and I can't." (P15, F, 60y, PGA=7.1, Non-Remission)
Fatigue	"I feel very tired, I do my job but in the end I feel exhausted (...) perhaps it is due to the disease... but I'm not sure, is it?" (P1, F, 72y, PGA=2.0, Non-Remission) "It's a fatigue even to talk." (P12, F, 47y, PGA=7.9, Near-remission)
Function	"Two weeks ago I could brush my hair but, in the meantime I stopped being able and had to cut it." (P31, F, 61y, PGA=9.9, Non-remission) "Lately I have to go down stairs with both feet on the same step." (P2, F, 55y, PGA=5.3, Non-Remission) "I couldn't tight the buttons in my clothes or even dress myself" (P26, M, 62y, PGA=invalid, Near-remission)
Stiffness	"In the morning I feel my joints very stuck for 2 hours and it's a lot harder for me to do my normal life as I used to." (P2, F, 55y, PGA=5.3, Non-remission)
Psychological well-being	"I worry more about the discomfort, feeling bad, than with the pain itself. (…) maybe it is more a psychological issue. I can't feel good about myself anymore." (…) "Your self-esteem is also affected and accounts to it" (P5, F, 59y, PGA=3.8, Near-remission)
Leisure limitations	"I pondered if I would be able to talk a walk by the sea, it wasn't the pain, it was the discomfort, how would I…? (P5, F, 59y, PGA=3.8, Near-remission)
Comorbidities and RA sequelae	"It's the lack of strength [in my hands], I still have sensitivity" (P14, M, 66y, PGA=, 7.5, Non-remission) "I thought, I do not know if it's because the medication but I get tremors. And at night I get up a lot because of the pain and because I can't find a comfortable position"(P24, F, 75y, PGA=NV, Non-remission) "I have pain in my arms but that's due to tendonitis, I should have had physiotherapy" (P32, F, 56y, PGA=0.6, Remission) "I have osteoarthritis all over the body" (P21, F, 73y, PGA=5.9, Near-remission)
Arthritis vs disease vs health	"Disease is a general thing. Here for example I noticed that it's only the arthritis that matters. Because if you have a colic, it's a disease, right?"(P5, F, 59y, PGA=3.8, Near-remission) "(...) this only refers to arthritis I don't have to include [the pain caused by an herniated disc]" (P27, F, 52y, PGA=4.5, Near-remission) "It's not that easy. It's almost all the same." (P27, F, 52y, PGA=4.5, Near-remission) "Sometimes we ask if the doctor wants us to evaluate our disease in general and he says no, that he only wants us to think about the arthritis" (P5, F, 59y, PGA=3.8, Near-remission)

PGA, Patient Global Assessment.

Remission is defined by SJC28, TJC28, CRP, and PGA all ≤1; Near-Remission, only PGA is >1; No-Remission, SJC28, TJC28, or CRP are >1. The Version 2 of PGA was considered for this definition.

Table 3. Quotes supporting the theme "Measurement Difficulties" and its different codes

Sub-theme	Codes	Quotes (Participant)
Scaling difficulties	"Is 100 good or bad?"	"— So you answered your health is very bad, wasn't it?" (Interviewer) — "No, here I answered [patient reads again PGA3] 100% is… oooh, it's worse! I'm sorry, I don't read… Can I change it? (…) I don't know, I thought that way because the other question was about the pain [PGA1 – disease], the pain was 100%. Here [PGA3] I thought the same way, your health is either 0 or 100%. That's my interpretation (…) that I was completely fine with 100%." (P3, F, 49y, PGA=2.2, Non-Remission) "So here the 100 is very well isn't it?(…) [looks at the question again] Here it's…it's the confusion that this is." (P6, F, 70y, PGA=2.0, Near-remission) "In this scale the 0 is good, the 100 is bad, it depends on the way you put it. In this case right here I always think that 100 is the good one." (P2, F, 55Y, PGA=5.3, Non-remission)
	"Is it 0-10 the same of 0-100?"	"Sometimes I don't understand the question. I don't understand if it's 0 to 10 or 0 to 100. I get confused with this, I don't know." (P6, F, 70y, PGA=2.0, Near-remission) "(…) usually I've to answer from 1 to 10" (P30, F, 61y, PGA=0.7, Remission)
	NRS vs VAS	"It's here? It's to write a mark? (…) Usually it's with the numbers, 0 to 100." (P5, F, 59y, PGA=3.8, Near-remission) "Usually it has the numbers (...) It's not like a straight line like this one." (P2, F, 55Y, PGA=5.3, Non-remission)
	Subjectivity of quantification	"Sometimes [the answers are not honest] because we [the patients] don't understand, because we don't know how to evaluate the pain itself." (P5, F, 59y, PGA=3.8, Near-remission) "… sometimes a person can be very well in the blood tests and have pain, I think…because it has happened to me, and the opposite, everything swollen and [the doctors] «so it's not hurting?» they push and it doesn't hurt." (P2, F, 55Y, PGA=5.3, Non-remission)
	"It can't be zero!"	"Usually I answer 2 or 3… sometimes I don't feel any pain at all, and I always answer 2 or 1, just by thinking of the day after. (...) We're always waiting for the worst!" (P2, F, 55Y, PGA=5.3, Non-remission) "No, it can't be 0. The psychic also counts, it's very important…" (P5, F, 59y, PGA=3.8, Near-remission) "(...) [I can ever answer 1] (…) look at my hand for example, this is all arthritis. If I have my self-esteem." (P6, F, 70y, PGA=2.0, Near-remission)
Time reference difficulties	Today vs Last week	"Uhhh the most adequate… may be this one ["Today"] Because in the last week the pain has already gone, and today I'm still feeling it (P28, M, 55y, PGA=2.2, Near-remission) "When we are told a week, we have to backtrack far behind and no longer intensify or decrease the pain. Because you are no longer feeling. And today when we get up in the morning, the space that takes us between morning and now ... is so recent." (P5, F, 59y, PGA=3.8, Near-remission) "I prefer this one «how I feel today» because it's simpler than remembering the other days (…) if I feel good today I try to forget what

		happened before.” (P30, F, 61y, PGA=0.7, Remission) "Today, compared to what I felt before ... Today I am much better (...) but maybe I did not think about the week that I felt less pain, I thought about a long time ago. (P3, F, 49y, PGA=2.2, Non-Remission) "I think ... it's more or less the same thing today or within the last week" (P8, F, 58y, PGA=1.3, Near-remission).

PGA, Patient Global Assessment.

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Table 4. Selection of quotes supporting the theme "Understanding the purpose of PGA" and their different codes

Codes	Quotes (Participant)
Not used to adjust the treatment	"I think it matters, for a better evaluation of the patient. And that it can influence (…) the treatment." (P28, M, 55y, PGA=2.2, Near-remission) "Honestly? I think the doctor sometimes asks that only as a routine – he doesn't really value it (…) Because at the same time, he's asking me that, he's already writing on the computer. He doesn't look me in the face. We only say yes or no." (P5, F, 59y, PGA=3.8, Near-remission) "I think it is important [the PGA]. The questions made are important because … sometimes if we have some disturbing situation, this medication [biological therapy] can't even be administered." (P8, F, 58y, PGA=1.3, Near-remission)
Only the doctor's judgment counts	"The doctor considers the blood analysis, evaluates the swelling, the spine movements and so on. And the question [PGA] is one more thing to have in account." (P19, M, 70y, PGA=invalid, Non-remission) "(…) We make the blood tests, the doctor does the [joint] counting, (…) if I give one answer that doesn't accord at all with that, obviously they might ignore me, or at least they become aware that we don't know what we have…" (P3, F, 49y, PGA=2.2, Non-remission) "Our correct and honest answer will help a lot in the analysis and the counting of the articulations. (P5, F, 59y, PGA=3.8, Near-remission) "If she [the doctor] thinks I'm worse she will increase the medication." (P15, F, 60y, PGA=7.1, Non-remission)
For research only	"[PGA fits out] To study, I don't know, I don't understand… why you [health professionals] ask that." (P2, F, 55y, PGA=5.3, Non-remission) "For me it's to evaluate. I think that is for them, for the doctors, to know if these recent treatments, in fact, worth or not." (P3, F, 49y, PGA=2.2, Non-remission)
Value of a structured explanation	"I didn't knew what was the purpose [of the PGA] (…) I knew the joints evaluation was to be possible for the doctor to see the evolution but I didn't knew the intention was to add that" (P3, F, 49y, PGA=2.2, Non-remission) "Although I always answered carefully because I knew it was important, I wasn't aware of its impact on the treatment." (P33, F, 42y, PGA=9.8, Near-remission) "I was somewhat aware because my husband likes to search and read. I have books to read (…) to get to know." (P1, F, 72Y, PGA=2.0, Non-remission) "Now that you're explaining it to me, I will take that into account in the next evaluation." (P2, F, 55y, PGA=5.3, Non-Remission)

PGA, Patient Global Assessment.

Remission is defined by SJC28, TJC28, CRP, and PGA all ≤1; Near-Remission, only PGA is >1; No-Remission, SJC28, TJC28, or CRP are >1. The Version 2 of PGA was considered for this definition.

Table 5. Disease activity and patient global assessment scores before and after the intervention

Patient number	Disease Activity				PGA scores (0 to 10cm)		
	TJC28	SJC28	CRP (mg/dl)	ACR/EULAR Boolean remission [a] Pre- and (-->) Post-Intervention	PGA pre-intervention[b]	PGA post-intervention[b]	Post- minus pre-intervention
P1	3	2	0.50	No	2.0	2.0	0
P2	3	2	1.02	No	5.3	5.7	+0.4
P3	3	0	0.02	No	2.2	2.2	0
P4	0	0	0.02	Near-Remission --> Remission	3.0	0.9	-2.1
P5	0	1	0.21	Near-Remission	3.8	2.0	-1.8
P6	0	0	0.30	Near-Remission	2.0	1.7	-0.3
P7	0	1	0.02	Near-Remission	1.1	2.4	+1.3
P8	0	0	0.02	Near-Remission	1.3	2.1	+0.8
P9	0	0	1.31	No	4.5	3.8	-0.7
P10	0	0	0.02	Remission	0.3	0.4	+0.1
P11	1	1	0.04	Near-Remission	4.9	3.7	-1.2
P12	0	0	0.13	Near-Remission	7.9	6.0	-1.9
P13	0	0	0.10	Remission	0.2	0.2	0
P14	2	2	0.27	No	7.5	8.2	+0.7
P15	2	0	0.27	No	7.1	8.0	+0.9
P16	4	0	0.93	No	6.6	7.5	+0.9
P17	1	1	0.57	Remission	0.2	0.3	+0.1
P18	0	0	0.23	Near-Remission	8.8	8.8	0
P19	2	2	1.8	-	NV	NV	-
P20	0	0	0.36	Near-Remission	1.9	1.5	-0.4
P21	0	0	0.51	Near-Remission	5.9	5.8	-0.1
P22	0	1	0.59	Near-Remission --> Remission	1.5	1.0	-0.5
P23	0	0	0.23	-	NV	NV	-
P24	0	0	1.20	-	NV	NV	-
P25	2	1	0.63	No	7.3	7.0	-0.3
P26	0	0	0.26	-	NV	NV	-
P27[c]	0	0	0.13	Near-Remission	4.5	3.2	-1.3
P28[c]	0	0	0.42	Near-Remission	2.2	1.9	-0.3
P29[c]	0	0	0.47	Near-Remission --> Remission	1.6	0.8	-0.8
P30[c]	0	0	0.20	Remission --> Near-remission	0.7	1.7	1.0
P31[c]	9	8	1.20	No	9.9	9.3	-0.6
P32[c]	0	1	0.26	Remission	0.6	0.6	0
P33[c]	0	0	0.07	Near-Remission --> Remission	9.8	0.2	-9.6
Total:	73% ≤1	85% ≤1	85% ≤1	Near-Remission = 52% (pre-) and 41% (post-intervention)	17% ≤1	28% ≤1	57% pre > post

ACR/EULAR, American College of Rheumatology/ European League Against Rheumatism; CRP, c-reactive protein; NV, not valid; PGA, Patient Global Assessment; SJC28, swollen 28-joint counts; TJC28, tender 28-joint counts.

a – Remission is defined by SJC28, TJC28, CRP, and PGA all ≤1; Near-Remission, only PGA is >1; No-Remission, SJC28, TJC28, or CRP are >1. The Version 2 of PGA was considered for this definition.
b –V2: "Considering all of the ways your arthritis has affected you, how do you feel your arthritis is today?"
c – These participates were interviewed individually