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Considerations and priorities for incorporating the patient perspective on remission in rheumatoid arthritis: An OMERACT 2020 special interest group report

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ABSTRACT

Objective: To determine how best to incorporate the patient perspective into rheumatoid arthritis remission criteria.

Methods: At OMERACT 2020, several studies, including a longitudinal multi-centre study testing the validity of adding patient-valued domains to the ACR/EULAR criteria, were presented and discussed by the virtual Special Interest Group.

Results: Overall consensus was that there is insufficient evidence to change the remission criteria at this point. Future work should focus on measurement of the new domain of independence, clarifying the value of the patient global assessment, and optimizing the input of domains that patients value in the criteria.

Conclusion: Incorporating the patient perspective into remission criteria should be further explored.

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Introduction

Remission is the desired outcome in rheumatoid arthritis (RA) treatment. At Outcome Measures in Rheumatology (OMERACT) 10 (2010), concerns were raised as to whether the American College of Rheumatology/European Alliance of Associations for Rheumatology (ACR/EULAR) remission criteria [2,10], including tender and swollen joint count, C-reactive protein and patient global assessment of disease activity (PtGA) adequately incorporate the patient perspective. The OMERACT 'Remission in RA: Patient Perspective' Working Group (WG) was formed to explore what patients consider to be essential criteria for describing remission, and whether this differs from the remission criteria used by ACR/EULAR [10]. The timeline of work in RA remission from 2006 to 2021 can be seen in Fig. 1.

First, qualitative focus groups were conducted to identify what remission (“disease activity as good as gone”) meant to people with RA [11]. Participants defined remission under three broad themes: reduction/absence of symptoms; reduction of impact of their disease; and a “return to normality” of life. Within these, a list of 26 domains were identified. Second, a survey study asked RA patients from six countries (n=274) to rank these 26 domains in order of importance [13]. Domains most frequently included in the top three by participants were: pain, fatigue, and independence. The third phase was to identify candidate instruments for these domains, and explore their value in assessing RA remission in an international longitudinal cohort study [8].

We aimed to explore how to best incorporate the patient perspective into RA remission criteria following the presentation of these data at OMERACT 2020.

Presenting evidence

This was an OMERACT special interest group (SIG) meeting, informed by primary and secondary research studies, presented below.

Scoping literature review: Two scoping literature reviews were conducted (led by Remission Fellow BJ) to:

1. identify any studies (qualitative and quantitative) that aimed to incorporate the patient perspective into an existing core outcome set for a long-term physical health condition.
2. identify any studies (qualitative and quantitative) that explored the patient perspective of the definition of remission in RA to

ensure the work of the remission group was still necessary and relevant.

In July 2019 comprehensive literature searches were conducted for both reviews using online databases: MEDLINE, EMBASE and CINAHL Plus, and reviewing citations from key publications in the field. For both reviews, the search strategy covered from 2011 (publication year of ACR/EULAR remission criteria) until July 2019 (when the searches were conducted). Both reviews only included results with adult participants, and had no limit on study design.

The search strategy for the inclusion of the patient perspective into a core set was: core set AND (patient perspective OR opinion* OR preference OR PRO* OR patient reported outcome*).

The search strategy for the patient perspective on remission in RA review was: remission AND rheumatoid arthritis AND (patient perspective OR opinion* OR preference OR PROM OR Patient-reported OR “Patient reported” OR PRO OR patient-evaluated OR “patient evaluated”).

CONSORT diagrams outlining the number of eligible papers at each stage for Searches One and Two are presented in Figs. 2 and 3 respectively. Search One identified three published papers from the OMERACT remission in RA working group [7, 12, 14]. Search Two did not identify any studies that aimed to incorporate the patient perspective into a pre-existing core set. Therefore, this review identified no substantial new evidence beyond the work of this group.

Meta-analysis of PtGA and remission. An individual patient data meta-analysis from 11 randomised controlled trials (led by Remission Fellow RF: [4]) concluded that the current remission definition that includes the PtGA, in addition to tender and swollen joint counts and C-reactive protein, performs better than a remission definition that excludes PtGA, for predicting a good functional outcome (change ≤ 0.0 units in the Health Assessment Questionnaire-Disability Index [HAQ-DI] from month 12 and 24). However, adding PtGA to the remaining three remission criteria reduced the predictive accuracy (sum of true positive and true negative rates) for good radiographic outcomes (from 51.1% to 40.5%), with a potential risk for overtreatment.

Longitudinal cohort study: A longitudinal cohort study of RA patients with low disease activity (Disease Activity Score 28 joint count [DAS28] < 3.2) or patient-perceived remission (i.e., answering ‘yes’ to the question “Would you say that at this moment your disease activity is as good as gone, yes or no?”) was led by Remission past-Fellow LR and Co-chair MB. Participants (n=246) were recruited from

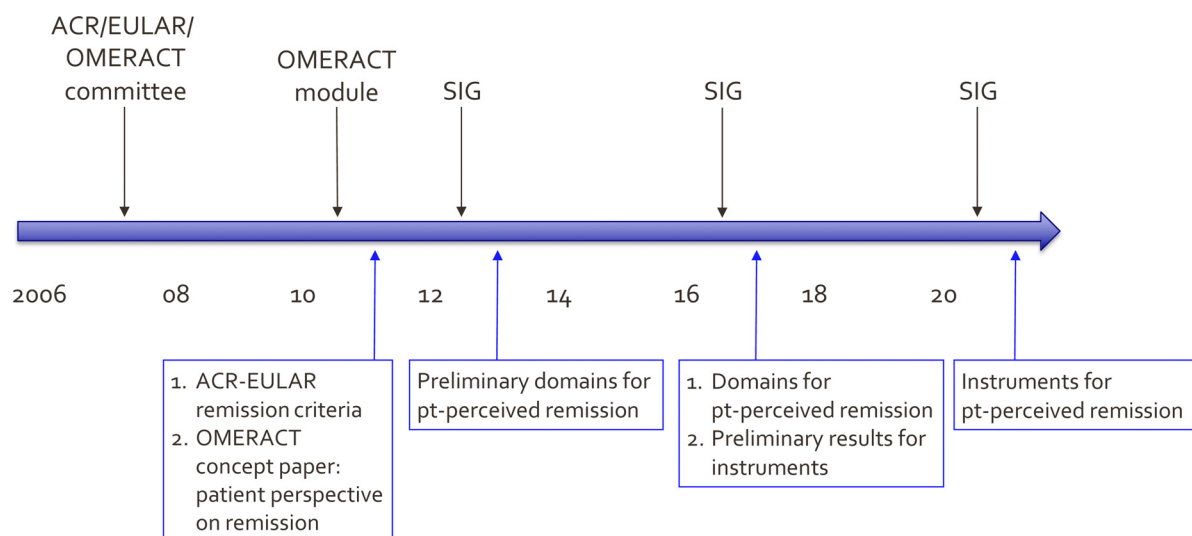


Fig. 1. Timeline of rheumatoid arthritis remission from 2006 to 2021.

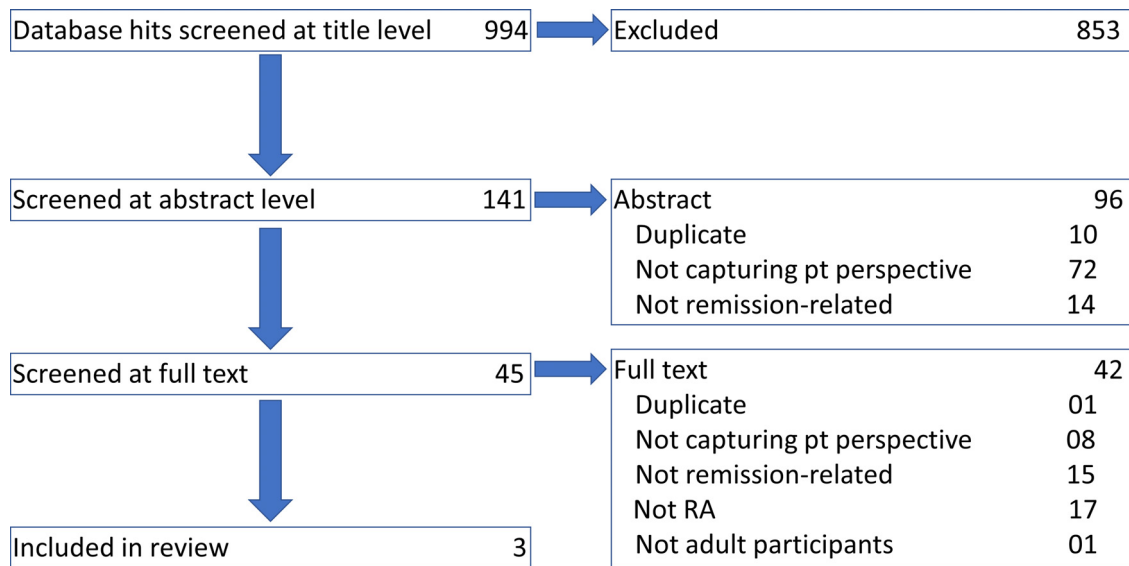


Fig. 2. CONSORT diagram for Search One: Patient perspective of RA remission.

four countries, with two sites providing longitudinal data at three (n=152) and six months (n=142). Validated instruments to measure pain and fatigue were selected, and a numerical rating scale was created to measure independence. These were tested in addition to ACR/EULAR Boolean-based remission (with and without PtGA) for prediction of functional outcome (HAQ-DI). Radiographic damage progression was an intended outcome measure but due to significant missing data was not analysed. Different disease activity scenarios (i.e., stable vs unstable in patient-perceived remission and in DAS28 < 2.6, at 0-3 and 3-6 months) were used and different sensitivity analyses were tested. Further details on this study can be found in the affiliated paper (Rasch et al, submitted).

Special Interest Group: 46 participants attended the virtual SIG (27th Oct 2020). Of these, 16 were patient research partners (PRPs). The WG’s previous research (described above) was summarized (CF), and MB presented a more detailed account of the longitudinal study findings and responded to questions. Delegates contributed to group

discussion either verbally or in a text chat stream running simultaneously throughout the meeting. At the end, a series of questions were posed to the attendees with the teleconferencing polling function used for voting (yes/no) (Table 1).

Group discussions

Independence

The measure used for independence in the longitudinal study is not validated, and therefore identified by the WG as a potential area of future research for discussion in the SIG. It was suggested that measurement of independence could be subjective and influenced by contextual factors such as access to social support networks and mobility aids, weather, time of day/year, and other conditions or injuries. Patients with longer disease duration and greater joint damage

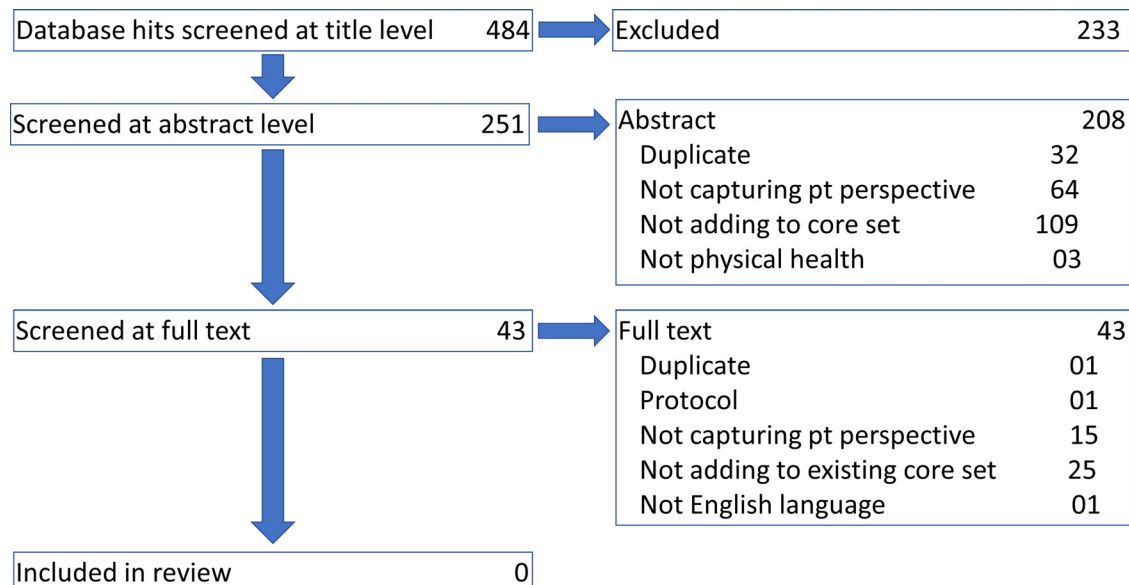


Fig. 3. CONSORT diagram for Search Two: Incorporating the patient perspective into an existing core set.

Table 1
Delegate voting results from virtual Remission SIG at OMERACT 2020.

Question	Weighted total Yes % (pPts + pHCP)/2 %	Total n=39 (%)		Patients only n=17 (%)		Professionals only n=22 (%)	
		Yes	%	Yes	%	Yes	%
Do you agree that...:							
a decision on the current criteria needs to be taken now?	24	10	26	2	12	8	36
there is insufficient evidence from the data to change the ACR/ EULAR remission criteria at this time?	91	36	92	14	82	22	100
independence is an important domain?	91	36	92	14	82	22	100
the current numeric rating scale for independence should be further validated?	90	35	90	16	94	19	86
Should we continue to work on patient global assessment?*	95	36	95	17	100	19	90

* NB: only 21 professionals completed the final question.

may have permanent loss of independence, which would reduce ability to reach remission:

"Achieving independence is wonderful and indeed what we are striving for, but as a domain for remission it then means that a patient with established RA will never be in remission, despite when pain and fatigue are gone" (patient delegate)

"Independence is a challenging one as loss of independence may still remain" (patient delegate)

A broader concept of independence that included quality of life and the ability to adjust to self-management was also discussed:

"I also wonder how much independence is helpful versus the term quality of life." (patient delegate)

"In a way I like to propose a new definition of health as 'the ability to adjust and to self-manage' more than the more global term 'independence'." (patient delegate)

Patient Global Assessment (PtGA)

The influence of the PtGA on determining remission in RA has received much attention in the literature [1, 6]. Overall, two main suggestions were made: 1. To increase the PtGA cutoff from one to two out of 10 for remission criteria [9], supported by data from the validation study (Rasch *et al.*, Submitted), which found a substantial proportion of patients in self-declared remission score their PtGA as two; 2. To develop a patient's perspective of remission criteria separate from the physician's perspective [3].

Some PRPs mentioned they were unsure how to consider impact of multiple conditions in the PtGA; and whether to take the domains of pain, fatigue, and independence into account when answering the PtGA. There was consideration of whether altering the anchor of the PtGA or to directly ask whether patients' RA was "as good as gone" might incorporate these domains identified as important from a patient perspective into remission criteria:

"As a patient with RA, I agree that my own criteria for the patient global score differs at times so I imagine each patient's criteria varies as well." (patient delegate)

"I never know what I should be thinking about when giving my patient global score" (patient delegate)

"It's hard to attribute fatigue to one disease over the other so the scale is always hard to complete" (patient delegate)

Factors influencing measurement of remission

Delegates noted that patients may not experience off-drug remission, highlighting impact of on- versus off-drug remission as an area for future research. The concept of modifiers for remission, including medication, was welcomed by many in the group.

"Why can't there be various modifiers/qualifiers for 'Remission' depending on context and trial? Time period, on/off meds" (Health professional delegate)

The duration of reduced or no symptoms was also raised by PRPs as important in defining remission. The existing criteria do not have specific requirements on time, and it was clarified that there was no agreement among patients in the initial focus groups regarding how long the RA symptoms would need to be absent for it to be considered RA remission [11], therefore duration was not taken forward into further studies by this WG. Further research may be needed to reach consensus on a minimum clinically relevant duration of no symptoms:

"It can also have a huge impact on someone being told they are in remission and understanding if they truly are in remission...or just having a good day" (patient delegate)

Wider implications

It was noted that while RA remission criteria are intended for use in clinical trials, they may have wider implications if used in clinical practice. For example, RA patients deemed to be in remission may be denied social security support or disability pension payments; or changes to employment duties or education may occur. Delegates were reminded that the goal of OMERACT is to develop outcome measures for clinical trials and while the criteria may filter into clinical practice, they are not intended for clinical practice:

"I don't like the term remission as people equate it with remission in cancer and think you can go back to work, stop benefits, etc." (patient delegate)

Result of voting during session

The SIG voted on five questions. Thirty-nine participants (including 16 PRPs) voted on questions 1-4, and 38 participants voted on question 5. Table 1 reports delegate voting results for the entire group including patient stakeholders as well as for patient stakeholders separately.

Delegates reached consensus that there is insufficient evidence from existing data to propose a change to the remission criteria (92%). However, consensus was also reached that independence is an important domain (92%) and that efforts should be made to validate a numeric rating scale for independence (90%) (Table 1). Additionally, consensus was reached that work should continue on the PtGA for remission criteria (95%).

Future of the working group and next steps

The Remission in RA: Patient Perspective WG has now met its initial aim to identify the domains that are important to patients regarding the concept of remission. The suggested future direction of the WG is to develop and test a measure of independence for RA, firstly through further qualitative work to explore how patients understand and define the domain of independence in more depth. Additional

work on the PtGA in relation to remission is also needed, but this may be beyond the scope of this WG and researchers have already begun to address this in the literature [4, 5]. Exploring the value of a separate patient-perspective measure of remission is also a potential area for future research, although this was not voted on in the SIG.

Conclusion

In conclusion, there is insufficient evidence from the current data to propose a change to the existing ACR/EULAR remission criteria. However, independence is an important domain in need of further research to clarify the meaning with patients and to identify the best way to measure this. Work should also continue on the patient global assessment in relation to remission.

CRedit author statement

Bethan Jones: Methodology, Investigation, Formal analysis, Writing – original draft, Writing – review and editing **Caroline Flurey:** Conceptualization, Methodology, Investigation, Resources, Writing – reviewing & editing; Visualization, Supervision; Project Administration **Susanna Proudman:** Methodology, Investigation, Resources, Writing – review & editing, Supervision, Project administration **Ricardo J. O. Ferreira:** Conceptualization, Formal analysis, Writing – Reviewing & Editing **Marieke Voshaar:** Conceptualization, Writing – Reviewing & Editing **Wijnanda Hoogland:** Conceptualization, Writing – Reviewing & Editing **Hema Chaplin:** Writing – Reviewing & Editing **Niti Goel:** Writing – Reviewing & Editing **Merete Hetland:** Writing – Reviewing & Editing **Catherine Hill:** Writing – Reviewing & Editing **Bindee Kuriya:** Writing – Reviewing & Editing **Kate Mather:** Writing – Reviewing & Editing **Linda Rasch:** Conceptualization, Methodology, Formal analysis, Investigation, Writing – Reviewing & Editing **Beverley Shea:** Methodology, Writing – Reviewing & Editing **Jasvinder A. Singh:** Conceptualization, Methodology, Writing – Reviewing & Editing, **Josef S Smolen:** Conceptualization, Writing – Reviewing & Editing **Jose AP da Silva:** Investigation, Writing – Reviewing & Editing **Savia de Souza:** Writing – Reviewing & Editing **Tanja Stamm:** Writing – Reviewing & Editing **Paul Studenic:** Writing – Reviewing & Editing **Maarten de Wit:** Conceptualization, Writing – Reviewing & Editing **Peter Tugwell:** Conceptualization, Methodology, Investigation, Writing – Reviewing & Editing **Maarten Boers:** Conceptualization, Methodology, Validation, Writing – Reviewing & Editing

Declaration of Competing Interests

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.semarthrit.2021.07.010.

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