RHEUMATOLOGY

Rheumatology 2015;54:615–622
doi:10.1093/rheumatology/keu379
Advance Access publication 16 September 2014

Original article

Stiffness is more than just duration and severity: a qualitative exploration in people with rheumatoid arthritis

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Abstract

Objective. Stiffness is internationally recognized as an important indicator of inflammatory activity in RA but is poorly understood and difficult to measure. The aim of this study was to explore the experience of stiffness from the patient perspective.

Methods. Semi-structured interviews conducted with 16 RA patients were analysed independently by researchers and pat.ient partners using inductive thematic analysis.

Results. Six themes were identified. Part of having RA identified stiffness as a normal consequence of RA, perceived as associated with disease-related aspects such as fluctuating disease activity, other RA symptoms and disease duration. Local and widespread highlighted stiffness occurring not only in joints, but also over the whole body, being more widespread during the morning or flare. Linked to behaviour and environment illustrated factors that influence stiffness, including movement, medications and weather. Highly variable captured the fluctuating nature of stiffness within and between patients and in relation to temporality, duration and intensity. Impacts on daily life emphasized the effect of stiffness on a range of domains, including physical function, quality of life, psychological well-being, activities of daily living and participation in work and leisure activities. Requires self-management detailed self-management strategies targeting both the symptom and its consequences.

Conclusion. Patients' experiences of stiffness were varied, complex and not exclusive to the morning period. Importantly, stiffness was reported in terms of impact rather than the traditional measurement concepts of severity or duration. Based on these findings, further research is needed to develop a patient-centred measure that adequately reflects inflammatory activity.

Key words: stiffness, rheumatoid arthritis, patient experience, qualitative.

CLINICAL SCIENCE

Introduction

RA is a chronic, systemic, inflammatory condition causing synovitis and resulting in pain, swelling and stiffness [1]. Morning stiffness (MS) is included in the original ACR classification of RA and remission criteria [2, 3]. Early MS (EMS) is considered an indicator of inflammatory activity and rheumatologists use stiffness as a crucial variable in decision-making for changing medication [4, 5]. MS is also widely used in RA research, particularly pharmacological trials [6], and is a key outcome in current research into timed-release glucocorticoid treatments [7, 8]. Stiffness in the inflammatory process is thought to be related to increases in pro-inflammatory cytokines such as IL-6 [9, 10].

Clinically, stiffness is frequently reported by patients [11, 12] and has considerable effects on daily life, work and quality of life [13–15]. However, these studies have generally focused on morning function, making it difficult to differentiate stiffness from pain and disability. In qualitative research by the OMERACT Flare Working Group, patients considered MS to be an important influence on

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Submitted 21 March 2014; revised version accepted 1 August 2014.

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decisions to seek medication review [16]. In the resultant combined international patient and professional Delphi exercise, stiffness was prioritized as a potential item for a core set of flare measures (79% consensus) [17]. Furthermore, in a recent qualitative study, patients highlighted stiffness reduction as a crucial aspect of RA remission [18].

Traditionally, assessment is through questions about EMS duration or severity. However, different question formats [visual analogue scales (VASs), numerical rating scales, Likert scales] for severity are not interchangeable and severity does not correlate with duration [19]. Patients who answer no to the presence of EMS have later reported its duration in minutes in a subsequent question, implying the questions are unclear [12]. Given these measurement difficulties, it is vital to understand the concept of stiffness from the patient perspective if we are to evaluate it effectively. Only one study has focussed on understanding the patient experience of stiffness [20], but it was conducted more than a decade ago, since when there have been substantial changes in RA treatment [21] and thus likely changes in stiffness experience. Furthermore, no validated stiffness measure has been developed using the recommended methodology including concept mapping through qualitative exploration [22]. Therefore the aim of this study was to explore the experiences of stiffness in patients with RA.

Patients and methods

Following ethics approval (Leeds East Research Ethics Committee, 13/YH00/50) patients with confirmed RA [2] and experience of RA-related stiffness were invited to participate in semi-structured interviews. Patients attending outpatient clinics at two National Health Service (NHS) trusts were purposefully sampled using a sampling frame to reflect a range of age, gender and disease duration.

An interview guide (Table 1) was developed based on a literature review and discussion with the research team (Table 2). Interviews and analysis followed an iterative process that allowed ideas and concepts identified in early analysis to be explored in subsequent interviews [23]. All patients gave informed consent and completed a disability questionnaire (HAQ) [24], perceived disease activity VAS [25] and pain VAS. All interviews were conducted by one researcher (S. Halls) who was unknown to participants prior to the study and introduced herself as a non-clinical researcher. Interviews were conducted with only the researcher and participant present except for one interview where the participant brought her young son. Interviews took place in non-clinical rooms, lasted between 30 and 80 min, were audio-recorded and then transcribed verbatim. Data collection continued until saturation was reached and no new themes were emerging.

Data were analysed using inductive thematic analysis, a method of identifying and reporting patterns in data without the use of an a priori model [26]. Data were managed using NVivo 10 (QSR International, Doncaster, VC, Australia) [27] and Microsoft Office Word 2007. Transcripts were read, re-read and systematically coded, then codes were explored for patterns, which led to theme development [26]. The interviewer (S. Halls) analysed all transcripts. Researchers (S. Hewlett, E.D.) independently analysed two transcripts, patient research partners [28] (G.B., A.E.), after a brief introduction, also read two transcripts and highlighted relevant points from their perspective, and discussions among the research team throughout the analysis process facilitated agreement on the developing codes and themes.

Table 1 Interview guide

A. Can you tell me about your experience of stiffness in relation to RA?
B. How does this vary in a 24 h period?
C. Has stiffness varied over the course of your disease?
D. How does stiffness differ from other RA symptoms?
E. What are the consequences of stiffness?
F. How do you deal with stiffness?
G. How do you assess stiffness?
H. Is there anything that you feel is important to stiffness that we have not talked about?

Results

Sixteen of 38 patients who were approached agreed to participate (42%): 11 female, aged 33–78 years, disease duration 1–27 years (Table 3). Analysis identified 219

Table 2 Study team characteristics

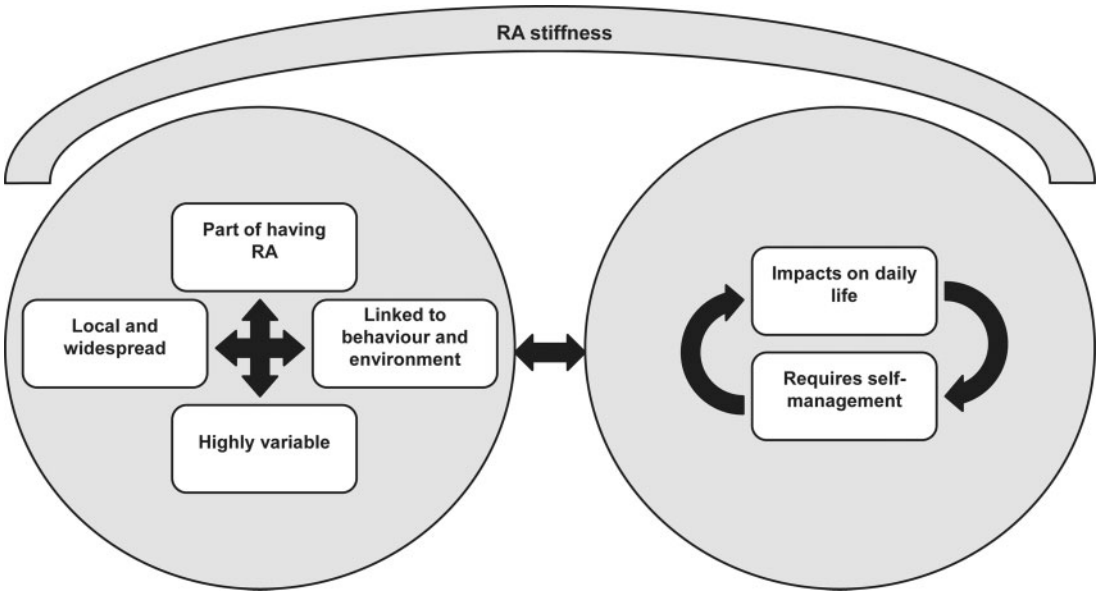
Team	Gender	Position	Years of rheumatology experience
S. Halls	F	PhD researcher	2 years
E.D.	F	Rheumatology psychology researcher	5 years
J.K.	M	Academic rheumatologist	>30 years
J.P.	M	Epidemiologist	>10 years
G.B.	F	Patient research partner	RA diagnosed ⩾10 years
A.E.	F	Patient research partner	RA diagnosed ⩽10 years
S. Hewlett	F	Academic rheumatology nurse	>20 years

TABLE 3 Individual participant demographic data

Patient ID	Gender	Age, years	Disease duration, years	HAQ	PtG	Pain	Current medication
101	Male	62	22	1.25	1.3	9.0	NSAIDs, DMARDs, glucocorticoids, biologics
102	Female	48	25	2.25	3.9	5.4	NSAIDs, DMARDs, biologics
103	Male	71	11	1.50	3.7	2.2	NSAIDs, glucocorticoids
104	Male	78	1	0.25	4.7	0.0	DMARDs glucocorticoids
105	Female	62	15	1.63	†	†	DMARDs, glucocorticoids, biologics
106	Female	62	2	1.13	†	†	DMARDs, glucocorticoids
107	Female	37	9	1.50	3.5	3.6	NSAIDs, glucocorticoids, biologics
108	Female	60	2	2.25	10.0	10.0	DMARDs
109	Female	33	3	2.13	1.6	5.8	NSAIDs, DMARDs, biologics
110	Female	63	7	2.50	4.9	4.9	NSAIDs, DMARDs
111	Male	74	7	1.50	1.8	5.2	DMARDs
112	Female	48	23	2.63	4.6	7.6	NSAIDs, DMARDs
113	Female	48	14	1.00	3.2	3.7	NSAIDs
114	Female	71	14	1.75	†	†	NSAIDs, DMARDs
115	Male	45	2	1.88	2.8	6.7	DMARDs, biologics
116	Female	55	27	1.00	6.5	7.7	DMARDs
Mean	—	57.3	11.5	1.63	4.0	5.5	—
S.D.	—	13.2	8.9	0.63	2.3	2.8	—
Range	—	33–78	1–27	0.25–2.63	1.3–10.0	0.0–10.0	—

HAQ: 0–3 (3 = severe disability); PtG: patient perceived global disease activity, 0–10 VAS (10 = severe disease); pain: 0–10; VAS: visual analogue scale, 0–10 (10 = severe pain); †: incomplete data.

FIG. 1 Conceptual diagram of the patient experience of stiffness



codes that were grouped into six themes (see Supplementary Table S1, available at *Rheumatology* Online) that captured the patients' experiences of RA stiffness (Fig. 1).

Theme 1: part of having RA

Patients considered stiffness to be part of their disease and a normal consequence of RA: 'All rheumatoid arthritis sufferers get used to a level of pain and a level of

stiffness which they consider to be normal' (Patient 101). RA stiffness was considered different from stiffness as a result of exercise, due to differences in location, occurrence and experience:

> For me, muscle stiffness used to be, because obviously it's associated with working out [. . .] it was like a nice ooh God yeah, I'm really stiff today [. . .] but with arthritis you know it's an on-going [. . .] so it's a negative stiffness. Because you, after a while, you don't realise this at the time, but it won't go away. (Patient 112)

Patients felt that stiffness varied with fluctuations in disease activity: 'it's much worse on a flare-up' (Patient 113). Patients who also had stiffness from joint damage indicated that stiffness from mechanical and inflammatory processes felt different in terms of severity and persistence:

> I suppose a joint that's gone over, it's knackered, is a restrictive stiffness and pain but a joint that's flared is a completely different feeling [. . .] once you've got damage, you're always stiff. (Patient 112)

Relationships with other RA symptoms were apparent, most significantly between pain and stiffness, which was stronger during flares:

> I think they are separate but when, you know, when everything's sore, everything's swollen and everything's stiff, it's all kind of you know, in a bag together and then you're just in a pickle really. (Patient 109)

Although some found it difficult to differentiate, most patients could discuss pain and stiffness independently and felt they were different yet related concepts: 'They're connected and related but they're not interdependent [. . .] if I've got stiffness it's not guaranteed I've got pain' (Patient 107).

For some patients, stiffness was particularly significant in early disease: 'My rheumatoid arthritis started just after [my son] was born [. . .] and it started with morning stiffness' (Patient 109). For others it appeared to be more prominent later in their disease duration: 'I used to have the morning stiffness only really. It's only really in the last few years that I've started getting evening stiffness as well' (Patient 107).

Theme 2: local and widespread

Patients considered stiffness to relate to joints: '. . . in the joint [. . .] and right deep in the joint' (Patient 110). Some patients highlighted that certain joints were affected, while others suggested the location varied over the course of their disease:

> It is a bit random, it does tend to move around, I might be sort of 6 months with it really bad in my feet and my knees and then I might find that it is worse in my back and hips and then it might move up to my shoulders and my elbows. (Patient 102)

For some patients, stiffness was described as being more of a whole-body experience, particularly during the morning or flare: '. . . stiffness when you're getting up, it feels like all up your arms and your legs and your whole body more' (Patient 116).

Theme 3: Linked to behaviour and environment

While patients related stiffness to their disease, they also associated it with their behaviour and environment. Stiffness was considered a result of both immobility: 'Oh it's always much more difficult to get up after sitting still' (Patient 103) and overactivity: '. . . if I have had a busy day, and I haven't been able to rest [. . .] then I might find that it is creeping back in the evening as well' (Patient 102).

Medications were perceived to influence the duration, severity and impact of stiffness: '. . . this morning it was about half an hour [. . .] and that's with taking the steroids, which does make it easier' (Patient 113) and

> I have been on the (Drug name A) now for just coming up to 3 months [. . .] I feel better but I still suffer with the stiffness, especially in the mornings. Whereas on the (Drug name B) I never suffered any of that, I just woke up in the morning and it was just like I was normal. (Patient 115)

Patients sometimes felt that the dramatic effect of medication on stiffness was ignored due to the lack of an appropriate assessment method:

> I kind of feel that it's sort of a lost entity because actually the drug is working, one of the things that they've really transformed has been my stiffness, but it's never been a measure that's kind of been considered [. . .] the one thing they've never asked me about is joint stiffness and the one thing I'm absolutely delighted about is that I can now get up and get him [my son] up whereas I haven't for two and a half years because I can't do that in the morning [. . .] and like the nurses all know and that's great but if they measured it they'd be brilliant because I could then say 'Yeah, look', you know? (Patient 109)

Some patients also suggested that cold and wet conditions accentuated stiffness duration, severity and impact: 'I suspect that today what with it being cold and so on, I'll probably continue to feel much as I do right now until possibly eight or nine at night' (Patient 103) and '. . . I do like the sunshine [. . .] I just feel not so stiff everywhere [. . .], whereas when it's tipping in rain I'm so blooming stiff I've got a job to move' (Patient 105).

Theme 4: highly variable

Patients emphasized the highly variable nature of stiffness, which varied in time, duration and intensity, within and between patients:

> . . . if you are an active person again your level of stiffness [. . .] would be different for somebody who sat down watching the television, or doing nothing or reading a book or whatever. They are going to get a lot more stiff than an active person. (Patient 101)

and

> . . . sometimes its only 10 minutes and I can get rid of it really quite quickly and then other times it is just hanging on and I just gradually just shed it through the first hour or so of the day. (Patient 102)

Although patients did relate stiffness to the morning period: '. . . stiffness, it's always there in the mornings, sometimes it's very bad' (Patient 103), the majority highlighted a broader, variable temporal pattern. They reported stiffness as lasting all day: '. . . the stiffness is there give or take 24/7. It comes and goes in waves as it were, but at the same time, it never really goes away' (Patient 110), or recurring in the evenings: '. . . I have the usual stiffer in the morning and stiffer at the end of the day' (Patient 107).

During flares, stiffness was described as 'an exaggeration of itself' (Patient 109). It was perceived to increase in duration:

> . . . [stiffness] will vary anything from about half an hour to, I have had up to about two/three hours, unless I've obviously had a bit of a flare up, then obviously it can be all day thereabouts. (Patient 107)

It was perceived as more severe:

> I can tell if I am going through a period when not being controlled very well cause the activity will increase [. . .] I am stiffer either first thing in the morning or getting towards tea time in the evening. (Patient 102)

It also had greater impact:

> Just everything I think when you get a flare and it's really bad. Again it's just your hands just don't work basically. They can't bend them, grip things, and obviously it's really painful and it makes everything awkward. When they are not so bad you can do basic stuff, you can pick up a kettle, you can do bits and bobs. There is a big difference between the two. (Patient 115)

Stiffness was also perceived to recur more frequently, including at night, and affect more joints: '. . . it's not just on a morning it's all throughout the night . . .' (Patient 113).

Theme 5: impacts on daily life

Patients evaluated their stiffness in terms of its impact rather than duration and severity. Physical function was considerably influenced by stiffness, including reduced mobility, balance, dexterity, grip and range and speed of movement: 'Just, I mean a job to move really, your limbs and your joints, your fingers. You can move them but they just, I just find it sometimes initially quite hard to do . . .' (Patient 106) and

> I mean it's like the other day I lost a screw out of my glasses and I could see this screw and it was down there, and do you think I could get my fingers to pick it up, I could not, I could not get my fingers to pick up this blooming stupid screw. (Patient 105)

Stiffness was highlighted as impacting on quality of life, and disruption of normality was stressed, as was impact on ability to work: 'I am not safe enough to be on a building site I don't think, I couldn't get up steps and stuff, things that I used to do' (Patient 102). Some patients experienced an improved ability to cope with stiffness as a result of retirement:

> . . . getting up to go to work was getting worse because it was taking longer to be able to get to move to be able to put the car in gear [. . .] but, I think now because I'm not working it's easier, I can cope with it better. (Patient 113)

Essential daily activities such as eating and dressing were highlighted as being particularly affected by stiffness:

> I'd end up eating a lot of soup because I just can't get my mouth open as wide to take even just a simple fork of food, and chewing just becomes a total non-starter. Yeah so I get joint pain in my jaw but also it's really stiff. (Patient 109)

and '. . . it's just when you're stiff you just find it hard to do, just to do stuff, whether it's something really simple, it just makes it so much more difficult basically' (Patient 115).

Participation in leisure activities and hobbies were restricted by stiffness:

> I'm making my step-daughter her prom jewellery at the moment and I can only do, whereas before I would've just made it in a night no problem at all but when I'm stiff [. . .] I can't do it because I can't pick up the bead or pick up the needle. (Patient 109)

Many patients described frustration as a result of the restrictions imposed by stiffness:

> . . . I can find it quite frustrating at times, especially when I really want to get something done by a certain time or by a certain day of the week, or because I've got something else happening I need to get that done. (Patient 107)

Patients also discussed how pain would result from carrying out movements restricted by stiffness:

> It's difficult one to inflict, no matter how, you must keep your range of movement, it's difficult when you are in pain to continuously move a joint into that position where it hurts. But then if you don't it gets stiffer. (Patient 102)

Theme 6: requires self-management

Patients articulated numerous strategies to self-manage stiffness and its consequences. Strategies targeted a range of domains and were both direct (targeting stiffness) and indirect (targeting the consequences of stiffness). Direct movement-based strategies included moving, stretching, moving while still in bed, and supporting or

manipulating joints. For example, '. . . before I get up out of bed I try to move all my joints just you know, while I am not actually standing up to actually just try and get everything moving a bit' (Patient 102) and 'Sometimes like this morning I had to physically bend my hands to get them to work because they just won't, they're kind of just locked' (Patient 115). Heat and cold techniques such as the use of hot showers and ice packs were employed by many patients to directly relieve stiffness: 'Whereas stiffness you can generally, you know like using hot and cold [. . .] you can work it out' (Patient 102) and 'First thing in the morning [. . .] hot water is wonderful. I can move then' (Patient 105).

Indirect strategies to manage impact included behaviour adjustment:

> People say 'oh that's a nice dress' and I think yeah it's because I couldn't get my jeans on but you know, thanks though [. . .] and you just do it, you don't really think it I suppose. You just adapt in the morning. (Patient 109)

Patients also described having to prepare and plan tasks, including getting going earlier to compensate for slower movements:

> I had to go for an MRI scan before Christmas [. . .] and that was about 10 o'clock in the morning, but it was the only one that they had and I thought well, I've just got to do it haven't I? I've just got to move myself a lot earlier. (Patient 105)

Patients also suggested that stiffness in a flare does not reduce with usual self-management techniques: 'So if I have a hot shower on a standard day I'm up and going [. . .] whereas on a bad day I can't get it to reduce as well, it just lasts and I can't shift it' (Patient 109).

For one, the only effective management was a steroid injection: 'So that's extreme stiffness, and I am not exaggerating that [. . .] it seems the only way to resolve that one is to have a massive injection of steroid' (Patient 101).

Discussion

Patients experience stiffness as significant, variable and complex. Stiffness was reported to be a normal part of having RA, experienced in joints and more widespread, related to behavioural and environmental factors and to have marked variability (including not being limited to early morning). It resulted in wide-ranging consequences that had a major impact on patient's daily lives and necessitated self-management.

Patients placed greater importance on stiffness impact than stiffness severity or duration. While impact was mentioned in earlier research [20], patient-reported outcome measures (PROMs) have continued to rely on non-standardized, unvalidated duration and severity questions. Although stiffness duration is most frequently assessed in trials [12], stiffness severity has been reported to have stronger correlations with relevant outcomes and inflammatory markers [29]. Severity and duration do not correlate [19] and a recent review of stiffness in low-disease states [30] shows the only two PROM validation studies make conflicting recommendations on whether severity or duration is best [29, 31]. It is therefore time to consider the potential effectiveness of measuring stiffness via concepts beyond severity and duration. The most compelling argument is for the impact of stiffness, which was how patients in this study defined and evaluated stiffness. This would fit with the impact triad, which recommends considering not only the severity of an outcome, but also its importance to patients and their ability to self-manage it [32].

These patient perspectives on stiffness might explain the poor performance of traditional stiffness questions. Duration questions generally ask about EMS using various baselines, including from awakening or from getting up, and various endpoints, including start of improvement, substantial improvement or complete resolution [31]. Importantly, patients in this study did not relate stiffness exclusively to early morning, which could explain their difficulty in trying to determine a start or end point. In addition, traditional simple questions assume (but do not specify) that patients evaluate stiffness related to inflammatory processes, yet patients in this study could identify differences in inflammatory and mechanical stiffness. Finally, in existing assessment there is no consideration of stiffness location, yet patients report stiffness in single and multiple joints, as well as widespread (non-joint) stiffness, which they consider more severe. In moving forward to the development of individual items for inclusion in an appropriate RA stiffness PROM, aspects such as these should be captured to enhance the clarity of the target concept [33, 34].

While this study included only 16 participants from two NHS trusts in the same city, the sample included a range of ages, gender, treatment regimens and disease durations. There may be cross-cultural differences in the perception of stiffness, which is an area for further research. Furthermore, data saturation was achieved [35]. A key strength of the study included the reliability of the findings through independent analysis by other members of the research team [36].

These data provide important information about a well-recognized symptom that has a major impact on patients' daily lives and that is used internationally both clinically and in research. Stiffness measurement to date is not standardized, is unvalidated, inconsistent and unreliable and has not been developed according to current standards including collaboration with patients [33, 34, 37]. The importance of collaboration was demonstrated in fatigue, where collaboration led to international consensus that it should be assessed in addition to the core set in RA trials and development of the Bristol RA Fatigue scales [38–41]. This current study has demonstrated the importance of stiffness to patients, including one patient who reported that the significant impact of her medications went unrecognized due to lack of an appropriate stiffness measure. Further research now needs to use these data to develop potential items for a stiffness PROM. Development and

validation of a stiffness PROM will open up the potential for stiffness to be included in the ACR disease activity core set (currently omitted because it cannot be measured with sensitivity or specificity) [42]. It would also address the OMERACT 2010 research agenda item for development of a stiffness PROM in relation to flare [43].

Rheumatology key messages

- For patients with RA who experience it, stiffness is an important and complex symptom.
- Patients with RA generally characterize and define stiffness by its impact rather than duration or severity.
- These data have implications for the development of an appropriate RA stiffness patient-reported outcome measure.

Acknowledgements

The authors thank the patients who participated in this research, as well as Dr Paul Creamer and the clinical teams who facilitated recruitment.

Funding: This work was supported by a PhD studentship funded by the University of the West of England, Bristol, UK (grant number 430B180).

Disclosure statement: J.K. has received support from Horizon Pharma to attend scientific meetings. All other authors have declared no conflicts of interest.

Supplementary data

Supplementary data are available at *Rheumatology* Online.

References

1 Arthur V, Hill J. The musculoskeletal system and rheumatic diseases. In: Hill A, ed. Rheumatology Nursing: A Creative Approach. Chichester: John Wiley & Sons, 2006:25–92.

2 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.

3 Pinals RS, Masi AT, Larsen RA. Preliminary criteria for clinical remission in rheumatoid arthritis. Arthritis Rheum 1981;24:1308–15.

4 Kirwan JR, Chaput de Saintonge DM, Joyce CRB, Currey HLF. Clinical judgment in rheumatoid arthritis. III. British rheumatologists' judgments of 'change in response to therapy'. Ann Rheum Dis 1984;43:686–94.

5 Soubrier M, Zerkak D, Gossec L *et al*. Which variables best predict change in rheumatoid arthritis therapy in daily clinical practice? J Rheumatol 2006;33:1243–6.

6 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.

7 Buttgereit F, Doering G, Schaeffler A *et al*. Efficacy of modified-release versus standard prednisone to reduce duration of morning stiffness of the joints in rheumatoid arthritis (CAPRA-1): a double-blind, randomised controlled trial. Lancet 2008;371:205–14.

8 Clarke LL, Jessop DS, Hunt LP *et al*. Alleviation of morning joint stiffness by low dose prednisone in rheumatoid arthritis is associated with circadian changes in IL-6 and cortisol. Int J Clin Rheumatol 2011;6:241–9.

9 Perry MG, Kirwan JR, Jessop DS, Hunt LP. Overnight variation in cortisol, interleukin 6, tumour necrosis factor α and other cytokines in people with rheumatoid arthritis. Ann Rheum Dis 2009;68:63–8.

10 Straub RH, Cutolo M. Circadian rhythms in rheumatoid arthritis. Implications for pathophysiology and therapeutic management. Arthritis Rheum 2007;56: 399–408.

11 Scott JT. Morning stiffness in rheumatoid arthritis. Ann Rheum Dis 1960;19:361–8.

12 Vliet Vlieland TP, Zwinderman AH, Breedveld FC, Hazes JM. Measurement of morning stiffness in rheumatoid arthritis clinical trials. J Clin Epidemiol 1997;50:757–63.

13 da Silva J, Phillips S, Buttgereit F. Impact of impaired morning function on the lives and well-being of patients with rheumatoid arthritis. Scand J Rheumatol. 2011;40:6–11.

14 Westhoff G, Buttgereit F, Gromnica-Ihl E, Zink A. Morning stiffness and its influence on early retirement in patients with recent onset rheumatoid arthritis. J Rheumatol 2008; 47:980–4.

15 Phillips S, Dow L. Impact of impaired morning function on quality of life in rheumatoid arthritis: results of an exploratory patient survey. Int J Clin Rheumatol 2012;7: 597–606.

16 Hewlett S, Sanderson T, May J *et al*. 'I'm hurting and I want to kill myself': rheumatoid arthritis flares is more than a high joint count—an international patient perspective on flare where medical help is sought. Rheumatology 2012; 51:69–76.

17 Bartlett SJ, Hewlett S, Bingham CO *et al*. Identifying core domains to assess flare in rheumatoid arthritis: an OMERACT international patient and provider combined Delphi consensus. Ann Rheum Dis 2012;71: 1855–60.

18 van Tuyl LHD, 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 2014 Feb 12. doi: 10.1136/annrheumdis-2013-204798. [Epub ahead of print].

19 Rhind VM, Unsworth A, Haslock I. Assessment of stiffness in rheumatology: the use of rating scales. Rheumatology 1987;26:126–30.

20 Lineker SA, Badley E, Charles C, Hart L, Streiner D. Defining morning stiffness in rheumatoid arthritis. J Rheumatol 1999;26:1052–7.

21 Smolen JS, Landewé R, Breedveld FC *et al*. EULAR recommendation for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs. Ann Rheum Dis 2010;69: 964–75.

22 Patrick DL, Burke LB, Powers JH *et al*. Patient-reported outcomes to support medical product labeling claims: FDA perspective. Value Health 2007;10:S125–37.

23 Ritchie J, Lewis J. Qualitative Research Practice. A Guide for Social Science Students and Researchers. London, UK: Sage, 2003.

24 Fries JF, Spitz P, Kraines RG, Holman HR. Measurement of patient outcome in arthritis. Arthritis Rheum 1980;23: 137–45.

25 van der Heijde DM, van 't Hof M, van Riel PL, van de Putte LB. Development of a disease activity score based on judgement in clinical practice by rheumatologists. J Rheumatol 1993;20:579–81.

26 Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol 2006;3:77–101.

27 QSR International. NVivo qualitative data analysis software. Version 10. Doncaster, VC, Australia: QSR International, 2012.

28 Hewlett S, de Wit M, Richards P *et al*. Patients and professionals as research partners: challenges, practicalities, and benefits. Arthritis Care Res 2006;55:676–80.

29 Khan NA, Yazici Y, Calvo-Alen J *et al*. Reevaluation of the role of duration of morning stiffness in the assessment of rheumatoid arthritis activity. J Rheumatol 2009;36: 2435–42.

30 van Tuyl LHD, Lems WF, Boers M. Measurement of stiffness in patients with rheumatoid arthritis in low disease activity or remission: a systematic review. BMC Musculoskelet Disord 2014;15:28.

31 Hazes JM, Hayton R, Silman AJ. A re-evaluation of the symptom morning stiffness. J Rheumatol 1993;20: 1138–42.

32 Sanderson TC, Hewlett SE, Flurey C *et al*. The impact triad (severity, importance, self-management) as a method of enhancing measurement of personal life impact of rheumatic disease. J Rheumatol 2011;38: 191–4.

33 Patrick DL, Burke L, Gwaltney CJ *et al*. Content validity—establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO good research practices task force report: part 1—eliciting concepts for a new PRO instrument. Value Health 2011;14: 967–77.

34 Patrick DL, Burke L, Gwaltney CJ *et al*. Content validity—establishing and reporting the evidence in newly developed patient-reported outcomes (PRO) instruments for medical product evaluation: ISPOR PRO good research practices task force report: part 2—assessing respondent understanding. Value Health 2011;14:978–88.

35 Guest G, Bunce A, Johnson L. How many interviews are enough? Field Methods 2006;18:59–82.

36 Mays N, Pope C. Rigour and qualitative research. BMJ 1995;311:109–12.

37 US Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, Center for Devices and Radiological Health. Guidance for Industry: Patient-Reported Outcome Measures. Use in Medical Product Development to Support Labeling Claims, 2009. www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM193282.pdf (21 August 2014, date last accessed).

38 Kirwan J, Minnock P, Adebajo A *et al*. Patient perspective: fatigue as a recommended patient centred outcome measure in rheumatoid arthritis. J Rheumatol 2007;34: 1174–7.

39 Nicklin J, Cramp F, Kirwan J, Urban M, Hewlett S. Collaboration with patients in the design of patient reported outcome measures: Capturing the experience of fatigue in RA. Arthritis Care Res 2010;62: 1552–8.

40 Nicklin J, Cramp F, Kirwan J, Urban M, Hewlett S. Measuring fatigue in RA: a cross-sectional study to evaluate the BRAF Multi-Dimensional questionnaire, visual analogue and numerical rating scales. Arthritis Care Res 2010;62:1559–68.

41 Dures E, Hewlett S, Cramp F *et al*. Reliability and sensitivity to change of the Bristol Rheumatoid Arthritis Fatigue scales. Rheumatology 2013;52: 1832–9.

42 Felson D, Anderson JJ, Boers M *et al*. The ACR preliminary core set of disease activity measures for RA clinical trials. Arthritis Rheum 1993;36:729–40.

43 Bingham C, Alten R, Bartlett S *et al*. Identifying preliminary domains to detect and measure RA flares: report of the OMERACT 10 RA Flare Workshop. J Rheumatol 2011;38: 1751–8.