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Clinical science

‘I couldn’t carry on taking a drug like that’: a qualitative study of patient perspectives on side effects from rheumatology drugs

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Abstract

Objectives: There is growing interest in collecting outcome information directly from patients in clinical trials. This study evaluates what patients with rheumatic and musculoskeletal diseases (RMDs) consider important to know about symptomatic side effects they may experience from a new prescription drug.

Methods: Patients with inflammatory arthritis, who had one or more prescribed drugs for their disease for at least 12 months, participated in focus groups and individual interviews. Discussions were analysed using reflexive thematic analysis.

Results: We conducted seven focus groups with 34 participants across three continents. We found four overarching and two underpinning themes. The ‘impact on life’ was connected to participants’ ‘daily life’, ‘family life’, ‘work life’ and ‘social life’. In ‘psychological and physical aspects’ participants described ‘limitation to physical function’, ‘emotional dysregulation’ and ‘an overall mental state’. Extra tests, hospital visits and payment for medication were considered a ‘time, energy and financial burden’ of side effects. Participants explained important measurement issues to be ‘severity’, ‘frequency’ and ‘duration’. Underpinning these issues, participants evaluated the ‘benefit–harm balance’ which includes ‘the cumulative burden’ of having several side effects and the persistence of side effects over time.

Conclusions: In treatment for RMDs, there seems to be an urgent need for feasible measures of patient-reported bother (impact on life and cumulative burden) from side effects and the benefit–harm balance. These findings contribute new evidence in support of a target domain—an outcome that represents the patient voice evaluating the symptomatic treatment-related side effects for people with RMDs enrolled in clinical trials.

Keywords: OMERACT, harms, safety, adverse events, core outcome set, rheumatology.

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Rheumatology key messages

- Various aspects are important to patients when evaluating safety from medical treatment.
- Patients suggest 'severity', 'frequency' and 'duration' to be important measurement issues when assessing side effects.
- Feasible measures of patient-reported bother from side effects and benefit–harm balance are urgently needed.

Introduction

The Consolidated Standards of Reporting Trials (CONSORT) harm extension provide guidelines on items to include in harm-reporting from randomized controlled trials (RCTs) [1]. However, benefits of interventions are more likely to be published from RCTs than harms [2, 3], and underreporting of harms concerns both patients and clinicians within rheumatic and musculoskeletal diseases (RMDs) [4]. Patients and clinicians value different aspects of harms [5, 6], i.e. clinicians aim to perceive signs of diseases while patients evaluate symptoms that are apparent to the patient [7], and consequently clinicians tend to underestimate the severity of patients' symptoms [8, 9]. However, the majority of information on harms collected in RCTs comes from clinicians' rather than patients' perspectives [10]. Thus, a new complimentary measure assessing patients' perspectives on safety is needed.

Outcome Measures in Rheumatology (OMERACT) is an international collaboration of clinicians, researchers, patient research partners (PRPs) and industry aimed at improving outcome measurement and instrument methodology across RMDs [11]. Established in 1992, the organization has successfully developed Core Outcome Sets (COS) for many RMDs [12, 13]. A COS is a minimum consensus-based set of outcomes that should be measured and reported in all RCTs of a specific health condition or intervention. In all COS, benefits and harms should be equally and explicitly included [13]. To assess harms in RMDs, the OMERACT Safety Working Group has previously developed Rheumatology Common Toxicity Criteria 2.1 providing guidance on harm collection and reporting in rheumatology RCTs from the clinician perspective [14]. However, a suitable measurement instrument to assess the patient perspective is lacking [15].

We consider 'harms' to be the totality of possible adverse consequences of an intervention; i.e. the direct opposite of benefits [1]. Studies commonly report 'adverse events'—a term also traditionally used within OMERACT when evaluating outcome domains [12]. However, in this study we used the term 'side effect' as this term is more widely used in lay populations and avoids the possibility of patients only focusing on the worst side effects. We also added the term 'symptomatic', which relates to a subjective manifestation (e.g. pain or discomfort) apparent to the patient themself but which might not be observable to the clinician [7].

At OMERACT 2018, the Safety Working Group presented and discussed results from international focus groups with inflammatory arthritis patients on concerns in DMARDs use. We found that patients and clinicians have different perspectives of side effects, and that the cumulative effect of 'nuisance side effects' can have substantial impact on patients' lives [16, 17], which can lead to discontinuation of treatment over time [18]. We further conducted a systematic literature review identifying a comprehensive list of side effects reported in RCTs within RMDs, which could be appropriate for patient-reporting [19], and we presented the list to patients in individual interviews [20].

The previous results emphasized the importance of developing one or more patient-reported measure(s) to complement clinicians' reports: these should include severity [19] and how patients view the balance between treatment benefit and harm [16, 17]. However, it was unclear what patients want to know about potential side effects prior to medical treatment, and which side effects are most important to them. It is critical to identify what should be measured in relation to side effects in clinical trials to support patients' treatment decision-making. The present study focuses on inflammatory arthritis—i.e. RA, PsA and axial SPA (AxSpA)—as they have similar characteristics [21] and many of the drugs used to treat are the same. To inform the development of a patient-reported outcome measure, this study aimed to define what constitutes the domain for patients' own reports of safety by evaluating what patients consider important to measure in RCTs in relation to potential symptomatic side effects from their rheumatological drug treatment.

Methods

Study design

International focus groups and interviews were conducted to explore a broad range of patients' experiences and opinions and promote discussion [22]. The study protocol is published online (Supplementary File S1, available at *Rheumatology* online, and www.parkerinst.dk).

Patients and setting

Patients were eligible to participate if they had a confirmed diagnosis of inflammatory arthritis (i.e. RA, PsA or AxSpA), were over 18 years of age, and had been taking one or more prescribed drug(s) (e.g. NSAID, DMARD, glucocorticoid) for their inflammatory arthritis for at least 12 months. We invited potential participants through the OMERACT community, and participants were encouraged to pass our study details to other relevant patients. Participants were purposively sampled to reflect a variety of age, gender, ethnicity, employment status, condition, disease duration and use of rheumatological medication.

Potential participants were given an information sheet (Appendix Box 1 in Supplementary File S1, available at *Rheumatology* online) and invited for an online one-to-one pre-meeting for further information and to get familiar with online meetings. We collected demographic and clinical data (Appendix Box 3 in Supplementary File S1, available at *Rheumatology* online), and participants completed a consent form (Appendix Box 2 in Supplementary File S1, available at *Rheumatology* online). After the focus groups, we invited 10 participants to individual interviews exploring patients' perspectives on relevance, comprehension, and adjustments to our preliminary list of patient-reported side effects. Results of the individual interviews are reported elsewhere [20].

Ethics approval

This study was carried out in accordance with the Helsinki Declaration. Permission was obtained on 14 March 2022 (confirmation number P-2022-94) from the Data Protection Agency of the capital region in Denmark, and data were handled according to agreements. Patients were asked to provide written informed consent to participate in this study.

Data collection

Building on our previous qualitative data related to patients' concerns in DMARD use [16, 17], and in discussion with PRPs (M.V. and P.R.), we developed a focus group guide with probing questions to facilitate discussions that was adjusted after the first focus group (Box 1). Discussions were iterative, where ideas raised were explored in subsequent groups. Although not all European participants were native English speakers, we conducted six focus groups in English and one focus group in Danish. The focus groups (average 1 h and 22 min) were conducted online by the main investigator (D.B.B.) supported by two qualitative researchers [C.A.F. (in English) or M.U.R. (in Danish)] from June 2022 to February 2023 using Microsoft Teams (version 16.2.8). Discussions continued until no new concepts were identified, and enough data were generated to give rich insights into these concepts [23]. Three to six focus groups should provide sufficient rich data to address our research question [24]. All discussions were audio-recorded, transcribed verbatim, anonymized and analysed.

Analysis

We analysed data using reflexive thematic analysis [22], which uses a bottom-up approach to search for common patterns (themes) within data without fitting the data into pre-existing coding frames or the researcher's preconceptions [25]. Data were managed using NVIVO (version 14).

To familiarize ourselves with the data, the first author (D.B.B.) read the transcripts multiple times searching for units of meaning to generate descriptive codes. Secondly, moving back and forth between the data set, we generated initial codes, explored codes for links, and systematically grouped them into larger concepts. In reflexive thematic analysis, one investigator coding across data is considered good practice for consistency in meaning-making. Our coding was primarily semantic (explicitly expressed meaning), and analysis was primarily inductive (data-driven). Third, we generated initial themes describing participants' broader shared meanings across the full data set. Fourth, we reviewed the themes and relationships between the themes ensuring they reflected important patterns of what participants considered important to know about side effects in RCTs. Fifth, a final review ensured that the themes were built around strong core concepts, and the final naming for each overall main theme was decided. Sixth, we ensured a faithful analytic narrative to our data in our final writing on finessing of the themes [22, 25].

We analysed all focus groups in the language of origin. Relevant quotes identified from Danish focus groups were subsequently translated into English. The Danish transcripts were coded and analysed by two investigators (D.B.B. and M.U.R.) independently, while one investigator (D.B.B.) analysed the English transcripts supported by another investigator (C.F.). The investigators reached comparable conclusions and subsequently agreed on all details for codes, concepts and themes by discussion.

Patient involvement

From the design and conceptualization stages to the manuscript submission stage, two PRPs (M.V. and P.R.) with experience in the OMERACT methodology have been involved in the study. Following guidelines from OMERACT [26], EULAR [27] and Guidance for Reporting Involvement of Patients and the Public 2 (GRIPP2) [28], patient engagement was prioritized.

Results

We were contacted by a total of 49 potential participants (Fig. 1). Of these, 34 were interviewed in one of the seven focus groups (three to six participants in each). Fourteen participants were from Europe, 11 from North America and 9 from Australia (Table 1). Participants had a mean age of 58 (range 21–81) years, and the majority were women ($n = 22$, 65%) and white ($n = 33$, 97%). Nearly 60% had RA, 20% had PsA and 20% had AxSpA. Mean disease duration was 23 years (range 2–50), and most were currently taking biologic DMARDs ($n = 24$, 71%), followed by conventional DMARDs ($n = 17$, 50%) for their rheumatological condition.

Thematic analysis identified four themes related to what participants considered important to know about potential symptomatic side effects from their rheumatological

Box 1. Interview guide for focus groups

1) What is the potential side effect(s) that worry you the most?
   a) Why does this(/these) side effect(s) worry you more than other side effects?
2) Before you decide about a new medical treatment for your disease, what would be important to know about potential side effects? (Probing: type of specific side effects, number of side effects, severity, impact on life/physical function/work/family/social interactions, fluctuation, duration.)
   a) Which of these items/outcomes related to side effects are most important to you?
   b) What makes that item/outcome related to side effects most important?
   c) Which one is the next most important to you?
3) How should we measure the cumulative burden of all combined side effects? (Probing: can we have one measure? Are more domains needed—which?)
4) Do you have anything else you would like to mention that we've not discussed?

medication: impact on life; physical and psychological aspects; time, energy and financial burden of side effects; and measurement issues. These were underpinned by patients having to weigh up benefits against harms, and the cumulative burden related to having two or more side effects at the same and the persistence of side effects over time (Fig. 2).

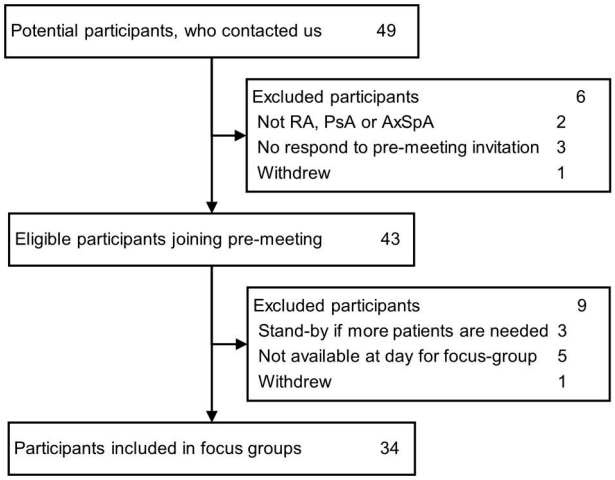

Figure 1. Flow diagram for participants included in focus groups. AxSpA: axial SpA

Impact on life

The impact of potential side effects on participants' lives was raised as an important issue in all focus groups.

> *'I would just say, that on the life-threatening thing, it's not so much worrying about whether you'll die from taking drugs, but it's about all the comorbidities that come with it'.* (Male, 54 years, AxSpA)

Participants explained that side effects impacted their ability to function in various roles, which affect their quality of life:

> *'If there was some way to measure, you know, the nausea, the fatigue—like it's keeping me from working—it's keeping me from studying—it's keeping me from whatever—it's affecting our quality of life'.* (Female, 52 years, RA)

Table 1. Demographic data for participants

	Overall ($n = 34$)	Australia ($n = 9$)	Europe and Middle East ($n = 14$)	North America ($n = 11$)
Age, years, mean (S.D.)	58 (14)	58 (11.3)	58 (13.6)	57 (16.2)
Gender, *n* (%)				
Female	22 (65)	7 (78)	9 (64)	6 (55)
Male	12 (35)	2 (22)	5 (36)	5 (45)
Ethnicity, *n* (%)				
White	33 (97)	9 (100)	14 (100)	10 (91)
Black	1 (3)	0 (0)	0 (0)	1 (9)
Employment status, *n* (%)				
Full time	6 (18)	2 (22)	3 (21)	1 (9)
Part time	8 (24)	3 (33)	4 (29)	1 (9)
Sick leave	1 (3)	0 (0)	1 (7)	0 (0)
Unemployed due to arthritis	4 (12)	1 (11)	0 (0)	3 (27)
Student	1 (3)	0 (0)	0 (0)	1 (9)
Retired	14 (41)	3 (33)	6 (43)	5 (45)
Diagnosis, *n* (%)				
RA	20 (59)	6 (67)	6 (43)	8 (73)
PsA	7 (21)	1 (11)	5 (36)	1 (9)
AxSpA	7 (21)	2 (22)	3 (21)	2 (18)
Disease duration, years (range)	23 (2–50)	24 (2–50)	26 (10–47)	19 (4–45)
Current use of rheumatological meds, *n* (%)				
NSAID	13 (38)	3 (33)	3 (21)	7 (64)
cDMARDs	17 (50)	4 (44)	9 (64)	4 (36)
Target DMARDs	1 (3)	0 (0)	1 (7)	0 (0)
bDMARDs	24 (71)	7 (78)	10 (71)	7 (64)
Glucocorticoid	13 (38)	1 (11)	4 (29)	3 (27)
Other	5 (15)	2 (22)	2 (14)	1 (9)
Prior use of rheumatological meds, *n* (%)				
NSAID	27 (79)	8 (89)	11 (79)	8 (73)
DMARDs	28 (82)	6 (67)	13 (93)	9 (82)
Target DMARDs	3 (9)	2 (22)	0 0	1 (9)
bDMARD	24 (71)	5 (56)	10 (71)	9 (82)
Glucocorticoid	21 (62)	6 (67)	8 (57)	7 (64)
Other	5 (15)	1 (11)	2 (14)	2 (18)
Comorbidities, *n* (%)				
Cardiovascular comorbidities	16 (47)	3 (33)	6 (43)	7 (64)
T2DM	1 (3)	0 0	0 0	1 (9)
Other comorbidities	29 (85)	7 (78)	13 (93)	9 (82)
No of meds for other conditions, median (range)	2.5 (0–11)	1 (0–6)	3 (0–7)	4 (0–11)

AxSpA: axial SpA; cDMARDs: conventional DMARDs; bDMARDs: biologic DMARDs: T2DM: type 2 diabetes mellitus.

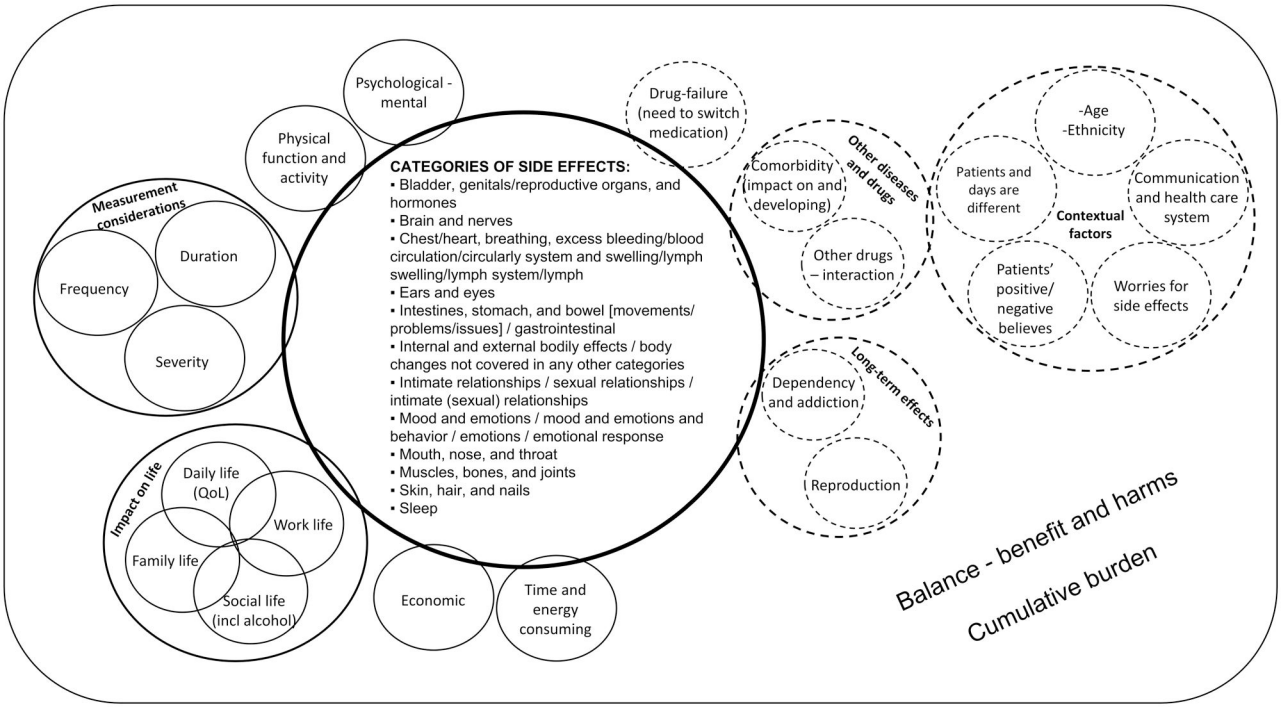

Figure 2. Patients perspective of important themes and sub-themes when assessing side effects in clinical trials.

It was important to participants that benefits offered by the medication to improve quality of life and live independently clearly outweighed side effects:

> *'For me this it's very important that the medicine—the side effects of the medicine—can give me at least what I consider a good quality of life—not to climb Everest or to walk more than 5 kilometres for something—but still just to be able to live my daily life and to be independent'.* (Female, 45 years, RA)

Participants described a substantial impact from multiple side effects on their ability to function and manage family life with children:

> *'I'm thinking about how it impacts my daily life and my ability to function with my family and at work. I've had lots of migraine and was losing weight, and then I also had some lung problems when I got the other treatment—sometimes you just have to pay the price'.* (Female, 33 years, AxSpA)

The impact of side effects on working life was crucial to some participants because they could risk losing their income and not be able to work:

> *'I think, really, for most people, depending on age, it's gonna be their work life, because you have to have income coming'.* (Male, 54 years, AxSpA)

Medication could further impact social life as some participants felt restricted in leaving their home:

> *'Being on the biologic, I've noticed some really explosive stomach reactions to some of the medications … just that consciousness of being at home on the day, you take that medication … And it's not necessarily something from a social point of view that you can necessarily explain to others than very close family. So, there's a social anxiety aspect as well'.* (Female, 64 years, RA)

Psychological and physical aspects

Participants discussed the aspect of side effects on both physical function and psychological wellbeing, and they seemed to consider both equally important:

> *'Maybe break it into physical and mental … It might be the extent to which it acts on your quality of life and your ability to function and do your everyday activities'.* (Female, 48 years, RA)

Participants described the physical aspect as limitations to their physical function or ability to do daily tasks due to side effects. Some participants reported experiences of their doctors not believing the severity of their physical side effects:

> *'I had problems with my lungs, my joints were fine … but suddenly I couldn't exercise like I use to—and exercise is usually my playground'.* (Female, 33 years, AxSpA)

> *'Fatigue and nausea, were very big for me … To the point where it got almost debilitating—I couldn't do like everyday things … I was trying to talk to my doctors about those side effects … [but] they didn't necessarily believe in the severity of the symptoms that I was having'.* (Female, 21 years, RA)

Psychological aspects included both emotional dysregulation such as mood swings and an overall mental state of feeling low due to the impact of physical side effects:

'The side effects keep coming and going—like in cycles, and sometimes—I'm definitely moody all the time, I can go through every move in the span of an hour'. (Female, 48 years, RA)

'When the lung thing kicked in, I literally feel like I lost everything: my identity—I had to go to a psychologist because I'm like … well, if I'm not this person who am I'. (Female, 47 years, PsA)

Participants often felt it could be difficult to distinguish side effects from other factors:

'So many of these drugs affect us … And we don't even realize that it's because of the drug'. (Female, 57 years, RA)

Time, energy and financial burden of side effects

To prevent side effects from medication, participants reported needing to have blood tests taken and go more regularly to their clinic or hospital. Some participants experienced side effects from their medication that leads to additional contact with other healthcare professionals. They explained that tests and visits take time and energy:

'What about all those visits you have to take to be tested to make sure that the side effects that you might have are or aren't occurring? … That's also like a side effect in the sense of the medication—methotrexate, you have to get blood tests, it takes time and energy'. (Female, 74 years, RA)

Some participants also found that the economic burden of paying for their inflammatory arthritis medication, or for the medication needed to treat side effects could impact them:

'One of the side effects that nobody ever really talks about is the financial side … They are horribly expensive'. (Male, 54 years, AxSpA)

Measurement considerations

Participants considered various aspects important to measure when assessing side effects. Three key issues were identified across participants: Severity, frequency and duration. It was important to participants to understand the potential severity of side effects as this could help them make decisions about managing their lives on their medication:

'I think it'd be more helpful for me to know—more like a level of fatigue, like extreme fatigue … because some of my [fibromyalgia] medicines cause such extreme fatigue, that I tried to adjust that within my time scheduled taking my RA medicines and some of them conflict, and then can cause other medical issues … So yeah, it'll just be nice to have like a tier system or levelling'. (Female, 52 years, RA)

Participants were also interested in knowing the risk of getting individual side effects, and would like to know which are the most common side effects before starting new medications:

'For me, it's important to know about the common side effects—about the frequency of desired effects—the probability that I can have of side effect'. (Male, 61 years, AxSpA)

The duration of a side effect also played a role, as participants were more prone to accept side effects if they knew the duration would be limited:

'I can live with nausea for a couple of weeks'. (Female, 60 years, RA)

Underpinning theme: balance between benefit and harms

Underpinning all these issues, participants were willing to accept a certain level of side effects if the benefit from the treatment was worth it:

'As long as the benefit is weighing out the risk, I'm probably still going to do it'. (Male, 62 years, AxSpA)

However, if participants felt that the side effects exceeded the benefit of their medical treatment, participants would discontinue their prescription:

'I had stopped taking it because not only was it making me really nauseous, but it also wasn't actually controlling the disease either'. (Female, 40 years, RA)

Participants were willing to continue with medical treatment if it could be adjusted leading to correct the benefit–harm balance:

'I couldn't carry on taking a drug like that no matter what … Then they suddenly said "Oh, you could have it injected" … and with the injection, the side effects were milder, and I was able to control them better … So, then I persisted with the methotrexate—otherwise I wouldn't have'. (Female, 74 years, RA)

Participants weighing up beneficial treatment effects against harms. Some participants explained they preferred to stay on a drug with severe side effects or long-term consequences as a dose reduction would make them sick:

'I weighed up my quality of life against possibly my life being a bit shorter by taking it. And I came to the conclusion that I would probably prefer to have a better quality of life than it to be longer … It wasn't worth living if I couldn't move and do what I wanted to do'. (Female, 60 years, RA)

Even though participants worried about potential side effects, they felt forced to seek medical treatment when they had worsening of their disease and symptoms:

'There was really no choice … I wasn't going to be able to live with that level of pain … In the situation I was desperate'. (Female, 46 years, RA)

Underpinning theme: cumulative burden

These findings are also underpinned by the concept that although some individual side effects might be minor, the

combined impact of several minor side effects as well as the persistence of side effects over time might have a substantial impact:

> *'It might appear to be smaller things, but it impacted my daily life a lot over the years when I had the wrong medication'*. (Female, 33 years, AxSpA)

Participants felt it was important to understand this cumulative burden on their lives. Whilst some participants were unsure on how cumulative burden should be measured, others suggested cumulative burden could be captured by measuring impact on life or quality of life, which might also include side effects occurring over time:

> *'If your hair's falling out and you're getting liver damage and you've got nauseous every time you take it, and you've got headaches at the same time… that's gonna have a huge impact… and in terms of getting back to your question about measuring that—that's hard'*. (Female, 48 years, RA)

> *'I think it would have to be something that says: cumulative burden of all of your side effects from this drug affecting quality of life or your daily life'*. (Female, 21 years, RA)

Discussion

This study found four overarching and two underpinning themes reflecting what patients find important to know about potential symptomatic side effects from their rheumatological medication. Impact on life and psychological and physical aspects were important, along with the time, energy and financial burden of side effects. Participants also considered the severity, frequency and duration of side effects important to measure. These findings were underpinned by patients weighting benefits against harms in deciding on whether to take medications or not—and by the cumulative burden of having multiple side effects concurrently well as the persistence of side effects over time. These issues are important to include in a new measure for side effects in addition to information that is already collected in clinical trials.

Our previous focus groups also found that patients balance the benefit–harm of medical treatment and experience a cumulative burden of side effects [16]. However, this study illustrates that patients' full experiences of side effects are not easily captured: it was unclear to patients how the cumulative burden should best be measured. Some participants suggested measuring impact on life or quality of life. Yet, this approach does not have a clear harmful direction, which challenge evaluating the balance between benefit and harm. Combining assessing three levels of benefit with three levels of harms has previously been suggested [29], but this simplistic approach might not adequately reflect patients' experiences [30]. Assessing side effects from a single measure is challenging, and a composite measure might capture both these multidimensions that patients have raised as important (physical and psychological aspects, life impact, frequency, duration and severity). However, in RA flare, it has been shown that a multidimensional construct can be captured with a unidimensional score [31].

Our findings support the COM-B health behaviour model [32]. This suggests physical and psychological ability to participate (Capability), external factors that make a behaviour possible (Opportunity) and the cognitive processes that inspire action (Motivation) all contribute to influencing health behaviour. Whilst all these factors contribute to understanding the health behaviour of medication adherence, our work focuses on drug side effects, which is a factor external to patients that affects the ability to take medication (opportunity). Participants also emphasized the importance of taking contextual factors into account such as health beliefs (motivation) or individual differences (capability). However, contextual factors are beyond the scope of this work, which focuses on treatment-related aspects (drug side effects). The 'Beliefs about Medication Questionnaire' may be useful in assessing the contextual factor of health beliefs. Studies have shown that RA patients with higher concerns about medication have increased risk of developing side effects and are less adherent to medication [33, 34]. Some participants in our study further worried about long-term drug consequences and were more prone to accept side effects if it would not permanently impact their life. However, contextual factors and long-term effects are closely examined by the OMERACT Working Groups of Contextual Factors and Patient-Outcomes-in-Longitudinal-Studies-in-RA, respectively, and are beyond the scope of this paper [35].

This study's strengths lie in rigorous qualitative methods, extending prior patients' perspectives on side effect. We included participants from three continents with diverse demographics and medication experiences. The proportion of women aligned with RA rates but were higher for PsA and AxSpA [36]—a more varied gender or diagnoses representation could have provided other insights. Most participants were white, possibly impacting the generalizability of patient perspectives as some ethnic minorities with inflammatory arthritis are less likely to achieve disease remission [37], which could relate to non-adherence driven by side effects. Using an online platform, we reached patients who otherwise would not have joined us (due to e.g. COVID-19 restrictions), but we may have missed those less confident using online technology. Still, we offered pre-meetings to support those less confident with online meetings. Translating only relevant quotes from Danish transcripts might limit understanding, but two Danish-speaking authors analysed the transcripts. Our study did not include patients with no or few side effects, mainly comprising experienced participants with long disease durations and (prior) glucocorticoid use, which are often associated with side effects [38]. Lastly, focus groups can be criticized for producing consensus opinion [39] but was chosen for its potential to elicit ideas through group discussion [40].

This study investigated what patients consider important to know about symptomatic side effects from medical treatment to inform the design of a patient-reported outcome measure. Patients emphasize the physical and psychological impact of potential side effects on their lives, considering both benefits and harms when accepting medication. Patients also want to understand frequency, severity and duration of side effects. The need for feasible measures of patient-reported bother (impact on life and cumulative burden) and the benefit–harms balance is urgent. These findings support a new target domain—an outcome that represents the patient voice evaluating the symptomatic treatment-related side

effects for people with RMDs enrolled in clinical trials. Next steps involve seeking agreement among patients and professionals on key issues raised in this study for developing such a measure.

Supplementary material

Supplementary material is available at *Rheumatology* online.

Data availability

The data underlying this article cannot be shared publicly due to the nature of qualitative data making it possible for participants to be recognized from context through full transcripts. While the sharing of illustrative quotes is covered by participant consent and ethics, the sharing of full transcripts is not.

Contribution statement

C.A.F., R.C. and D.B.B. conceived the study and developed the protocol. D.B.B., M.U.R. and C.A.F. collected the data. D.B.B. and M.U.R. did the analysis and interpreted the results from the Danish focus groups, and D.B.B. supported by C.A.F. did the analysis and interpreted the results from the English focus groups. D.B.B. and C.A.F. drafted the manuscript. All authors critically revised the manuscript for important intellectual content and approved the final version of the manuscript. R.C., T.E. and D.B.B. obtained funding. D.B.B. and C.A.F. are the guarantors.

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