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**European Qualitative research project on Patient-preferred outcomes in Early Rheumatoid Arthritis (EQPERA): rationale, design and methods of a multinational, multicenter, multilingual, longitudinal qualitative study**

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-023606
Article Type:	Protocol
Date Submitted by the Author:	14-Apr-2018
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Keywords:	Rheumatoid Arthritis, QUALITATIVE RESEARCH, Longitudinal study, Patient Preference

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Manuscripts

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3 **European Qualitative research project on Patient-preferred outcomes in Early**  
4 **Rheumatoid Arthritis (EQPERA): rationale, design and methods of a**  
5 **multinational, multicenter, multilingual, longitudinal qualitative study**  
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54 **Word count: 5100**  
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## ABSTRACT

**Introduction:** Including the patient perspective is important to achieve optimal outcomes in the treatment of rheumatoid arthritis (RA). Ample qualitative studies exist on patient outcomes in RA. A Belgian study recently unraveled what matters most to patients throughout the overwhelming and rapidly evolving early stage of RA. The present study, European Qualitative research project on Patient-preferred outcomes in Early Rheumatoid Arthritis (EQPERA) was created to contribute to a more universal understanding of patient-preferred health and treatment outcomes by integrating the perspectives of patients with early RA from three European countries.

**Methods and analysis:** In EQPERA, a qualitative, explorative, longitudinal study will be implemented in The Netherlands and Sweden, parallel to the methods applied in the previously conducted Belgian study. In each country, a purposive sample of patients with early RA will be individually interviewed 3-6 months after start of the initial RA treatment and subsequently, the same participants will be invited to take part in a focus group 12-18 months after RA treatment initiation. Data collection and analysis will be independently conducted by the local research teams in their native language. A meta-analysis of the local findings will be performed to explore and describe similarities, differences and patterns across countries.

**Ethics and dissemination:** Ethics approval was granted by the responsible local ethics committees. EQPERA follows the recommendations of the Declaration of Helsinki. Two main papers are foreseen (apart from the data reporting on the local findings) for peer-reviewed publication.

**Key words:** Rheumatoid Arthritis, Qualitative research, Longitudinal study, Patient Preference

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- The specific nature of the study, in which qualitative studies are carried out in different countries and languages using a uniform methodology, is novel, and we report in a transparent way about our approach and challenges.
- As no formal meta-analysis method was present in literature applicable to our study, we developed a method based on established techniques for the synthesis of qualitative research, which can guide other researchers interested in conducting this type of research.
- Several quality enhancing strategies are applied to yield sound results in this multinational, multilingual, longitudinal qualitative study.
- The participating countries might have rather similar cultural views and healthcare systems, which would strengthen the Belgian findings, however, the study protocol offers a methodological framework for research in different parts of the world.

## INTRODUCTION

In rheumatoid arthritis (RA), the outcome landscape dramatically changed over the past decades. RA is the most prevalent chronic, auto-immune inflammatory joint disease. It was typically described as an inevitably progressive disease with a destructive and disabling natural course. The continuous growth in effective pharmacological treatments contributed to this change, but the introduction of early therapy was one of the main drivers of transformed health outcomes of patients with RA.<sup>1</sup> Nowadays, remission or at least low disease activity have become realistic treatment targets for a notable proportion of the population.<sup>2</sup>

Nevertheless, the burden of disease and unmet needs remain considerable.<sup>3 4</sup> For example, most of the patients are at working age upon diagnosis, but work disability rates remain high.<sup>5</sup> Furthermore, patients with RA indicated the need for greater emotional support, and greater psychological support to manage the impact of disease on domains such as pain, fatigue, work and leisure.<sup>6 7</sup> Hence, it seems that patient preferences are not sufficiently understood and met by health professionals. In a recent report, patient-centered care was identified as a recurrent unmet need across rheumatic diseases, including RA.<sup>8</sup> Patient-centered care can be translated as care that is guided by the values and preferences of the patients,<sup>9</sup> with patient preferences referring to the perspective, beliefs and expectations of patients regarding their health and life.<sup>10</sup> As patient-centeredness is acknowledged as one of the key dimensions of high-quality care,<sup>11</sup> integrating the patient perspective in outcome assessment is increasingly advocated to achieve optimal outcomes in the treatment of RA.<sup>12</sup>

<sup>13</sup>

Qualitative studies shed light on the different views that patients with RA have on outcome compared to health professionals. These studies revealed the importance of fatigue and independence, among others, <sup>14-16</sup> to consider in daily practice on top of the traditional measures of disease activity, i.e., the swelling of joints and laboratory parameters of inflammation. Remarkably, limited attention has been given to the perspective of recently

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3 diagnosed patients. The early disease stage is probably the most daunting period for  
4 patients, indicating specific needs and preferences.<sup>17 18</sup> The Belgian qualitative study of Van  
5 der Elst et al. provided new insights into patient-preferred outcomes in early RA, concluding  
6 that returning to 'normality' as soon as possible was the core preferred outcome, which  
7 related to aspects of disease control and participation, physical and mental aspects.<sup>19</sup>  
8 However, understanding is lacking about the transferability of these local findings to other  
9 settings and cultures.  
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18 Despite recommendations for RA management, literature shows that there are differences in  
19 how rheumatology services are viewed and practiced across countries.<sup>20 21</sup> These differences  
20 may be attributable to characteristics of the national healthcare systems, local customs,  
21 practices, and values. Such cultural differences may consequently influence how patients  
22 evaluate their disease. For example, the survey study of Van Tuyl et al. demonstrated that  
23 the country in which patients were sampled resulted in slightly different key domains on how  
24 they perceived remission of disease.<sup>22</sup> Hifinger et al. showed that country of residence had  
25 an important influence on how patients with RA experienced fatigue.<sup>23</sup> It can thus be  
26 questioned whether patients in other countries would bring out other preferred outcomes.  
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38 To examine the transferability of the Belgian findings and to contribute to a more universal  
39 understanding of patient-preferred outcomes, we initiated the EQPERA consortium.  
40 EQPERA is the acronym for European Qualitative research project on Patient-preferred  
41 outcomes in Early Rheumatoid Arthritis. It is a multicenter, multilingual, longitudinal  
42 qualitative study across Belgium, The Netherlands and Sweden. The present paper reports  
43 about the international study protocol, based on the Belgian study procedures.  
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## 52 Objectives

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3 The overall research objective in EQPERA is to explore how local context influences patient-  
4 preferred health and treatment outcomes throughout the early disease course by integrating  
5 the perspectives of patients with early RA from three European countries.  
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8 The objective is twofold:  
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- 10 (i) to describe patient-preferred outcomes in early RA and how they change  
11 throughout the early disease course (national objective);  
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13 (ii) to identify differences, similarities and patterns in patient-preferred outcomes  
14 across the three European countries (international objective).  
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## 20 **METHODS AND ANALYSIS**

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22 The Belgian study was conducted during 2012-2013.<sup>19</sup> Based on the lessons learned and  
23 after multiple discussion rounds with the EQPERA steering group, an improved research  
24 protocol was written with the aim to implement a protocol as similar as possible in the other  
25 countries. Start of patient inclusion was 2016 in The Netherlands and 2017 in Sweden.  
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### 31 **Study design**

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33 A qualitative, explorative, longitudinal research design will be applied within a European  
34 context. As we study a research domain still lacking evidence, the use of qualitative methods  
35 is justified because we will learn from the rich descriptions of participants being shaped in  
36 their local contexts.<sup>24 25</sup> Longitudinal designs are relevant for studying complex phenomena  
37 and are specifically applicable in the context of a recent diagnosis since patients' perceptions  
38 and expectations may change during the overwhelming and rapidly evolving early disease  
39 stage. Previous research also suggests that the way patients experience and evaluate their  
40 disease can differ depending on disease duration.<sup>15 26 27</sup>  
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52 Patients with early RA will be invited to participate at two time points (Figure 1). At  $t_1$ ,  
53 participants will be individually interviewed 3-6 months after they have started their initial  
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3 treatment for RA. At  $t_2$ , participants will be invited to take part in a focus group 12-18 months  
4 after RA treatment initiation. To address a potential dropout of participants at  $t_2$ , those who  
5 decline to participate in a focus group will be invited for a repeated individual interview  
6 instead. However, the preferred interview method at  $t_2$  remains the focus group method to  
7 align with the original design of the Belgian study.  
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14 The reason for selecting different interview methods at  $t_1$  and  $t_2$  is based on the input of  
15 patient research partners and aims to match with patient preference in the context of a recent  
16 diagnosis. At  $t_1$ , the individual interview method is chosen because adjusting to a recent  
17 diagnosis can be seen as a primarily individual matter. Consequently, sharing personal  
18 experiences and opinions in a group setting can be too confronting at that stage of disease.  
19 A timeframe of 3-6 months after initiation of the initial RA treatment is chosen to not interfere  
20 with the diagnostic and therapeutic procedures, however, still including patients' earliest  
21 views on preferred outcomes. Furthermore, it is assumed that a few months of experience  
22 with the disease and treatment would help patients to communicate more easily about their  
23 outcome preferences.  
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36 At  $t_2$ , focus groups are chosen above the individual interview method for two reasons. Firstly,  
37 compared to the first interview moment, participants may probably feel more comfortable in a  
38 group setting, because of a grown disease perspective and the potential interaction with  
39 other patients (e.g., in the waiting room) by then. Secondly, group interactions potentially  
40 help participants to remember significant events and bring out personal thoughts, which in  
41 turn may result in more and diverse data.<sup>25 28</sup> It is reasoned that after 12-18 months of  
42 treatment experience, participants have had sufficient time to develop their view on the  
43 disease, with perhaps an observable change in their preferences accordingly.  
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## 54 **Research context**

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3 EQPERA involves three countries in Northwest Europe: Belgium, The Netherlands and  
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5 Sweden. These countries have a comparable organized healthcare system including a  
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7 comprehensive social security system, however, differences exist in for example their  
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9 reimbursement and referral system.

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12 Participants will receive usual care according to local standards. Across countries, a  
13  
14 comparable early RA management is implemented in respect of current international  
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16 guidelines.<sup>29 30</sup> patients should be treated (i) early: as soon as the diagnosis is made; (ii)  
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18 intensively, with methotrexate in the first treatment if possible; (iii) to target: treatment  
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20 adjustments according to a predefined target of sustained remission or low disease activity.  
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22 In addition, there is a common culture across the countries regarding interdisciplinary team  
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24 care as key in disease management, but diversity can be expected concerning  
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26 implementation aspects. For example, it has been shown that there is a wide variation in the  
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28 role of nurses in the management of patients with chronic inflammatory arthritis<sup>20</sup>, and in the  
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30 composition of rheumatology multidisciplinary teams<sup>31</sup>.

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34 In each country, an early RA cohort is available, the local teams include experienced  
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36 qualitative researchers with a good command of the English language, and funding  
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38 possibilities are available to work out their national project. The EQPERA steering group  
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40 consists of team members with different disciplinary backgrounds: nurses (KE, IL, EM, YH),  
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42 physiotherapists (AB, AG), a psychologist (JV), a patient representative (AG) and a  
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44 rheumatologist (RW).

### 45 46 47 48 **Level of collaboration between countries**

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50 Individual projects will be conducted in each country. The studies in Sweden and The  
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52 Netherlands will be led by the local principal investigator (IL and EM, respectively) and  
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54 supervised by the EQPERA project leader (KE), who designed and completed the Belgian  
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56 qualitative study.<sup>19</sup>

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5 Considering qualitative studies, potential language issues can be approached in two ways:  
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7 either translate the transcripts and do the analysis in one place, or have the analysis done at  
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9 each location and combine the data afterwards. We decided that (i) data will be collected in  
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11 the local settings by the local teams in their native language; (ii) interviews will be transcribed  
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13 in the original language and the transcripts will be analyzed by the local teams; (iii) only the  
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15 results of the local analysis (i.e., interpreted data) will be combined for EQPERA purposes,  
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17 and this after ending the analysis procedures and writing up the findings and conclusions in  
18  
19 every country.  
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22 Original data will thus not be reviewed by the other teams (Figure 1). Centralizing data would  
23  
24 mean translation of local transcripts to the common language in EQPERA (English).  
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26 Translation holds the risk of losing the real meaning of words,<sup>32</sup> and would be expensive and  
27  
28 time consuming because of the mountains of words that will be produced in every country.  
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30 Above and beyond translation issues, we assumed that local data should ideally be analyzed  
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32 by the people who are familiar with the local culture and context in order to get the most  
33  
34 appropriate interpretations.  
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### 36 37 38 **Collaboration with patient research partners**

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40 As EQPERA aims to capture the patient perspective, the project would benefit from active  
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42 collaboration with patient representatives, or those who have the lived experience of RA.  
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44 Following the recommendations of the European League Against Rheumatism for the  
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46 inclusion of patient representatives in scientific projects,<sup>33</sup> each local team will preferably  
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48 collaborate with two patient research partners.  
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52 The local principal investigators will be responsibility for coordinating this research  
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54 partnership, being guided by the FIRST (i.e., Facilitate, Identify, Respect, Support and Train)  
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56 framework of Hewlett and colleagues.<sup>34</sup> The exact level of the patient researchers'  
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3 contribution will depend on local agreements (feasibility). In general, they will help by  
4 reflecting on the methods, formulating clear and understandable interview questions,  
5 interpreting and explaining data, and providing feedback on the readability of the patient  
6 information leaflet and informed consent form.  
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## 10 11 12 **Participants**

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14 Eligible patients will have to meet the following inclusion criteria: (i) confirmed diagnosis of  
15 RA, in accordance with the American College of Rheumatology/European League Against  
16 Rheumatism 2010 criteria;<sup>35</sup> (ii) time between diagnosis and start of RA treatment of less or  
17 equal than 1 year; (iii) minimum age of 18 years; (iv) speak, read and write the local  
18 language; (v) started the initial RA treatment 3-6 months ago.  
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## 26 27 **Sampling**

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29 Every country will strive to include a broad range of perspectives in their sample. To ensure  
30 this variation, participants will be purposively sampled based on their (i) age/life phase; (ii)  
31 gender; and (iii) treatment progress/treatment experience. Moreover, every country will apply  
32 a multicenter recruitment to account for possible variation in region.  
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39 Sampling in qualitative research corresponds to the assumption that collected data is of  
40 sufficient depth, i.e., representing the various views and opinions of the population with no  
41 added value of including more participants for answering the research question.<sup>36 37</sup> As there  
42 is no standardized definition of data saturation, we decided that data collection can be  
43 stopped if three consecutive interviews do not result in new themes or additional  
44 understanding (local team decision).  
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52 At  $t_1$ , we estimate that around 20 participants in every country will be needed to reach data  
53 saturation. At  $t_2$ , the sample sizes will foremost depend on the interest and willingness of  
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3 participants to participate again. We aim for 4-8 participants in each focus group, which  
4 seems an appropriate number to keep the discussions manageable and stimulate  
5 contribution of every group member.<sup>36 38</sup> If possible, patient characteristics will be taken into  
6  
7 account to create a mix of perspectives in the groups.  
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## 10 11 12 **Recruitment**

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14 In each country, patients are recruited from multiple centers across different geographic  
15 locations, including academic and non-academic rheumatology centers. In Belgium, patients  
16 were sampled from nine centers across Flanders. The participating centers in The  
17 Netherlands are located in Nijmegen and Woerden, and in Sweden these are located in  
18 Lund, Malmö and Halmstad. A recruitment template will help the local teams to consider the  
19 main variables for creating heterogeneity in their samples.  
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## 29 **Data collection**

### 30 31 The interview guides

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33 The semi-structured interview guides include pre-defined topics, with open-ended questions,  
34 and probing questions to reach a higher level of detail. All questions relate to the central  
35 interview question: 'Which outcomes of your illness and antirheumatic treatment are  
36 important to you at this moment?'. In every country, the interview guides will have the same  
37 content at start, and main questions will be fixed across countries. Data collection and  
38 analysis will be performed simultaneously, making it possible to adapt the interview guides if  
39 necessary to increase participants' understanding or to reach data saturation (local team  
40 decision). If adaptations are needed, these will be documented in the local research journal.  
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51 The content of the interview guides is inspired by previous qualitative studies on outcomes  
52 from the patient perspective.<sup>14 16 39</sup> In EQPERA, Dutch and Swedish versions of the Belgian  
53 interview guides (Flemish language) will be prepared by the local teams. Given similarities  
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3 between the Flemish and Dutch language, minor adaptations will be applied after discussion  
4 and consensus with the Belgian team. Forward and backward translation will be used to  
5 prepare translations to English and Swedish (Figure 2).<sup>40 41</sup> The main interview questions and  
6 the interview procedures are elucidated in Supplementary file 1.  
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### 10 11 12 Individual interviews ( $t_1$ ) 13

14 At  $t_1$ , individual, face-to-face interviews will be conducted by maximum 2 interviewers per  
15 country, who are not involved in participants' clinical care. As the patient research partners  
16 noted that patients are in general not used to talk about outcome preferences, they will be  
17 asked to prepare written key words regarding the central interview question. The interviewer  
18 will start by elaborating on these key words. It is anticipated that interviews will last no longer  
19 than 60 minutes.  
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### 28 29 Focus groups ( $t_2$ ) 30

31 Focus groups will be facilitated by one of the interviewers of  $t_1$  in assistance of at least one  
32 participating observer. The focus groups will consist of three rounds: Round 1: preparatory  
33 phase; Round 2: (i) round-robin listing, (ii) developing a group list of patient-preferred  
34 outcomes, (iii) eliciting personal preferred outcomes, (iv) eliciting preferred outcomes in the  
35 actual stage of RA; Round 3: exploring the view of participants on the evolution of their  
36 patient preferred outcomes over the past year. The second round of the focus groups was  
37 inspired by the Nominal Group Technique methodology (NGT).<sup>42</sup> NGT is a consensus  
38 method that creates two types of data: (i) written ideas and prioritization, and (ii) the wider  
39 discussion, generating and clarifying ideas.<sup>43</sup> Our interest for using a prioritizing methodology  
40 is firstly, to create discussion between participants about a potential inconvenient topic; and  
41 secondly, to capture participants' underlying reasoning regarding preferences in outcomes. It  
42 is anticipated that focus groups will last about 60 minutes.  
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### Individual interviews ( $t_2$ )

If necessary, the interviewer of  $t_1$  will conduct individual interviews at  $t_2$ . The interview guide for these interviews is slightly adapted compared to  $t_1$  in order to question participants about their view on changes in their preferred outcomes over time.

### Procedures at both time points

Both individual interviews and focus groups will be held at a neutral and convenient location, and will be audio-recorded and transcribed verbatim according to transcription guidelines.<sup>44</sup>

Prior to the (focus group) interview, participants will document socio-demographic information. After the interviews, they will report about their general health, level of pain and fatigue during the past week on a visual analog scale. Clinical information will be extracted from the medical records by the local health professionals and shared with the local principal investigator.

### Data analysis

Data analysis will be conducted at two levels: (i) the local analyses of  $t_1$  and  $t_2$  data, followed by the longitudinal analysis; (ii) the meta-analysis with locally interpreted local data. The process of data analysis was based on several frameworks, which is summarized in Figure 3.

### The local analyses

In every country, the analysis process will be a team activity involving patient representatives. Preferably two researchers, including at least the local lead investigator, will independently code the interview transcripts. Data analysis will start after the first interview or focus group.

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3 The local researchers will follow the steps that are presented in Qualitative Analysis Guide of  
4 Leuven (QUAGOL) to analyze the interview data of  $t_1$  and  $t_2$ .<sup>45</sup> The central activity in  
5 QUAGOL is the constant comparison process: between researchers' interpretations and the  
6 actual participant story, as well as to check new ideas for their presence in previous  
7 interviews. QUAGOL divides data analysis into two phases.  
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12 The first phase suggests five steps of preparation, implying only paper and pencil work: 1)  
13 rereading of the transcript to get knowledge of what the interview is about, and highlighting  
14 the relevant fragments; 2) preparing a narrative summary by describing the key story lines  
15 close to participants' words; 3) schematically describing the key ideas of the interview in a  
16 conceptual scheme; 4) fitting test and adaptation of the conceptual scheme by going back to  
17 the transcript; 5) looking for common ideas/concepts across conceptual schemes as a first  
18 comparison with the other interviews.  
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26 The second phase comprises another five steps, representing the actual coding process: 6)  
27 creating a common code list, without hierarchical structure and based on the insights from  
28 the refined conceptual schemes; 7) coding of each significant passage in a qualitative  
29 software program, while critically reviewing and refining the introduced code list; 8) defining  
30 the concepts by looking across-cases and reviewing all citations connected to a concept; 9)  
31 integration of all concepts in one story line that answers the research question, followed by  
32 verification of this overarching framework against all interviews and interview schemes; 10)  
33 describing the results.  
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44 QUAGOL is not specifically developed for focus group analysis. Therefore, the group  
45 process will also be analyzed (i.e., how the conversation in the group is organized,  
46 developing and changing), as well as the differences within and between the groups will be  
47 taken into account.<sup>25</sup>  
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54 For the longitudinal analysis, the local teams will merge their data of  $t_1$  and  $t_2$ , in which  
55 meaningful individual statements will be extracted and compared between time points. There  
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3 are no universal frameworks for analyzing longitudinal qualitative data. The local teams will  
4 be guided by the method described by Saldaña,<sup>46 47</sup> who developed a 16-question template  
5 including (i) framing questions to help focusing on the context and conditions that influence  
6 changes over time; (ii) descriptive questions to describe what kinds of changes occur; and  
7 (iii) analytic and interpretive questions to reach richer levels of analysis.  
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### 14 The meta-analysis

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16 The findings of the three independently performed qualitative studies will be combined in a  
17 meta-analysis. Several methods for synthesizing qualitative studies have been developed,<sup>49</sup>  
18 with some studies also using a combination of methods.<sup>50</sup> The methodology developed for  
19 EQPERA is inspired by the principles of meta-ethnography as practiced by Britten et al.,<sup>48</sup>  
20 and by the coding process of QUAGOL (preparatory phase) that is based on grounded  
21 theory principles.<sup>45</sup> We combined key methodological elements of both approaches and  
22 summarized these into four steps: 1) describing each case; 2) recognizing differences,  
23 similarities and patterns across cases; 3) disentangling differences and similarities across  
24 cases; 4) fitting-test of the meta-interpretations.  
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36 The findings of the participating countries will be integrated by face to face interaction  
37 between the different local teams about their data in a consensus meeting. Local findings will  
38 be translated into English. The local teams of Belgium, The Netherlands and Sweden will at  
39 least consist of the principal investigator, a patient research partner and a rheumatologist to  
40 achieve an interdisciplinary view and prevent bias due to solo interpretations. A senior  
41 researcher of the EQPERA team (YH), who is not linked to the local teams and data, will  
42 moderate the meeting. Below, we describe our stepwise approach.  
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### 51 *Step 1: Describing each case*

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3 In step 1, the aim is to understand the course and results of each study on its own. Each  
4 country will be viewed as a case, with each case reflecting the overarching story of all local  
5 participants.  
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8 The lead investigators (KE, IL, EM) will present their findings (including quotes) and  
9 conclusions, covering: (i) the name and description of the patient-preferred outcomes; (ii)  
10 when, where, why, and in which circumstances they were put forward by the participants; (iii)  
11 the change through time of the description participants attached to the different outcomes.  
12 Furthermore, they will report about study details, using three short reports:<sup>45</sup> 1) a descriptive  
13 report, including what is specific to the participants, the treatment strategy, the research  
14 group and the healthcare system; 2) a methodological report, including deviations from the  
15 protocol, such as modifications to the interview guide, recruitment problems and level of data  
16 saturation; 3) a content report, including the main message derived from the data. A standard  
17 form will be used to enhance uniformity across presentations. The three cases will be  
18 presented one by one without immediate cross-comparison. After the case description, local  
19 teams will have familiarized with the other team's data and the particular context in each  
20 country.  
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34 In preparation of step 2, each team will individually reflect upon the following questions to  
35 stimulate the across-case analysis: 'What do I hear in every case?', 'What do I only hear in  
36 our case?', 'What do I not hear in our case?'. Furthermore, they will write down the patient-  
37 preferred outcomes they identified (codes and concepts) on color-coded sticky notes, each  
38 country representing another color, to support visually the comparison of the local findings in  
39 step 2.  
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### 48 *Step 2: Recognizing differences, similarities and patterns across cases*

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50 In step 2, the aim is to translate concepts from one study to another,<sup>48</sup> to determine how  
51 studies are related (i.e., what emerges across cases) and to recognize what is typical for  
52 each case.  
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3 An affinity diagram will be created to organize the multinational data.<sup>51</sup> The patient-preferred  
4 outcomes of the three studies will be displayed side by side (using the color-coded sticky  
5 notes). Their meaning will constantly be compared from one country to another in order to  
6 identify common and recurring, as well as conceptually different outcomes. We will start with  
7 a small set of concepts including the higher level concepts of each study, after which we will  
8 refine our first interpretations by discussing the lower-level codes.<sup>45</sup> During this process  
9 similar outcomes will be grouped if possible (by replacing the sticky notes), and we will look  
10 specifically for subtle differences between grouped outcomes.

11  
12 After reaching consensus on similarities and differences, a 'saturation grid' will be completed  
13 in preparation of step 3. This is a technique used in qualitative studies to identify covered  
14 (sub)themes in each interview and decide on data saturation.<sup>52</sup> However, we will use a  
15 prespecified grid to identify the coverage of outcomes across the three studies.<sup>48</sup> Firstly, the  
16 grouped outcomes will be renamed. Secondly, all outcomes will be listed, meaning that each  
17 outcome of each local study is encompassed by one of the renamed outcomes in the grid.  
18 The main explanation of each outcome will be added. Thirdly, each country will represent a  
19 column and their sticky notes will be pasted next to the outcome in the grid that fits best the  
20 description on the sticky note. Hence, the empty cells will represent the outcomes that do not  
21 emerge across countries. By completing the grid, an overview will be developed of  
22 differences and similarities across cases.

### 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 *Step 3: Disentangling differences and similarities across cases*

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44 In step 3, the aim is to explain the recognized differences and similarities by discussing why  
45 (or why not) certain outcomes emerge in a particular country or across countries.

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47 Starting from the saturation grid (step 2), we will first go back to the methodological  
48 considerations and contextual features (step 1), before looking for possible cultural  
49 explanations. The group discussion will be an essential element in this step. For this reason  
50 we will view this discussion as a focus group, producing data that will be audio recorded and  
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3 transcribed verbatim. After step 3, we will have obtained consensus on cross-cultural  
4 variation in patient-preferred outcomes in early RA.  
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6 In preparation of step 4, the local teams will separately draft a written summary of the  
7 discussion immediately after the focus group and with special attention to how their case was  
8 similar or different to the other cases.  
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#### 12 13 14 *Step 4: Fitting-test of the meta-interpretations*

15 In step 4, the aim is to verify the appropriateness of the interpretations made during the focus  
16 group (step 3) regarding similarities and differences across countries.  
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22 Each local team will perform a fitting-test of common and own meta-interpretations with their  
23 local data. The local researchers will go back to their data, after rereading the focus group  
24 transcript and with their written summary in mind. Two questions will need to be answered:  
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26 (1) Do the contextual interpretations actually reflect what is seen in our data? Is certain  
27 context information overlooked in the focus group? (2) Can we support the meta-  
28 interpretations with quotes that typically describe the perspective of our participants? During  
29 conference call meetings, the meta-interpretations will be adapted, completed or refined  
30 based on the fitting-test in each country.<sup>45</sup>  
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#### 40 **Enhancing data quality and methodological rigor**

##### 41 **Quality assurance**

42 EQPERA is a large, multicountry, multicenter, multilingual, longitudinal qualitative research  
43 project. To yield sound results, several strategies are applied to ensure trustworthiness.  
44 These are: (i) recruitment of a qualified and motivated team; (ii) use of forward-backward  
45 translation procedures; (iii) uniformity in recruitment, conducting the interviews and focus  
46 groups, transcription of audio files, data coding, data storing, and reporting; (iv)  
47 interdisciplinary team analysis (v) training of local staff to the protocol and hands-on  
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3 guidance by the project leader. In Table 1, a detailed description is provided of the used  
4 strategies according to four quality criteria (i.e., credibility, dependability, confirmability, and  
5 transferability).<sup>53 54</sup>  
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## 10 Quality appraisal

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12 As the findings of independently performed primary studies will be combined, quality is an  
13 important aspect to consider requiring a formal system for appraisal. The local teams will use  
14 a quality reporting tool to support a consistent use of methods and documentation across  
15 studies. Johnson et al. provided a useful template,<sup>51</sup> based on the consolidated criteria for  
16 reporting qualitative research,<sup>55</sup> and the quality criteria suggested by Mays and colleagues.<sup>56</sup>  
17 In EQPERA, several items were added regarding data management and quality appraisal in  
18 qualitative research.<sup>32 44 57-59</sup> Our tool comprises 50 items regarding four domains: 1)  
19 research team and reflexivity; 2) study design; 3) analysis and findings; 4) data management  
20 strategies (Supplementary file 2).  
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**Table 1** Applied quality assurance strategies in EQPERA, described for each research stage, according to Lincoln and Guba's framework for evaluating trustworthiness.<sup>53</sup>

Research stage	Employed strategies for supporting trustworthiness	Assessing quality:			
		(1) How congruent are the findings with reality? (2) Would the research findings be the same if the study would be replicated in essentially the same way? (3) Do the research findings emerge from the context and the respondents and not solely from the minds of the researchers? (4) Can the research be applied in other contexts?			
		(1) Credibility (internal validity)	(2) Dependability (reliability)	(3) Confirmability (objectivity)	(4) Transferability (generalizability)
<b>Study design</b>	<ul style="list-style-type: none"> <li>- developed around the patient perspective and in collaboration with patient representatives</li> <li>- triangulation of interview methods</li> <li>- addressing potential drop-out at <math>t_2</math></li> </ul>	•	•	•	•
<b>Establishment of the EQPERA team</b>	<ul style="list-style-type: none"> <li>- recruitment of a qualified team, with a passion for the topic:                             <ul style="list-style-type: none"> <li>o skilled in conducting qualitative research</li> <li>o familiar with the patient population</li> <li>o including patient research partners</li> </ul> </li> </ul>	•	•	•	•
<b>Protocol development and implementation</b>	<ul style="list-style-type: none"> <li>- a clear understanding of the overall project objective by all co-workers</li> <li>- use of detailed study protocol, including a methods and analysis plan, an interview protocol, a data management plan, and templates</li> <li>- training of local staff to the protocol (project leader) prior to patient recruitment of <math>t_1</math> and data collection of <math>t_2</math></li> <li>- monitoring of local progress and hands-on guidance (project leader)</li> <li>- documentation of local decisions (use of a research journal):                             <ul style="list-style-type: none"> <li>o when, why, what changes, and who was involved in making this decision (e.g., modifications to the interview guide)</li> <li>o personal and/or practical comments</li> </ul> </li> </ul>	•	•	•	•
<b>Sampling and recruitment</b>	<ul style="list-style-type: none"> <li>- purposive sampling informed by simultaneous data collection and analysis</li> <li>- multicountry and multicenter recruitment</li> </ul>	•	•	•	•

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- applying a definition for data saturation • •
- use of an enrollment template to support heterogeneity in the local samples and systematically keep records • •

**Data collection**

- semi-structured interview guides: • • •
  - o the same main interview questions in every country
  - o collaboration with patient research partners to support clarity and understandability of interview questions
  - o forward-backward translation
  - o the same key points in the introduction
- use of a data collection template and at least 2 audio recorders/interview to prevent missing data •
- verbatim transcription of the audio-recorded data •
- use of transcription guidelines •
- neutral and convenient interview location •
- $t_1$  - maximum 2 interviewers/country •
- maximum 2 interviews/day per interviewer to avoid interview burden and take time to reflect upon each interview
- $t_2$  - the interviewer of  $t_1$  is moderator of the focus groups •
- 1 moderator/country and the same observer(s) for each focus group

**Data analysis**

**Local level**

- independent coding by at least 2 researchers • •
- data collection and analysis in parallel •
- constant comparison method •
- use of field notes • •
- reflection after each interview/focus group: descriptive, content and methodological report • •
- use of a qualitative software program •
- peer debriefings: more frequently early in de coding process • •
- looking at data from multiple perspectives, including collaboration with patient researchers to help understand and describe the data • •
- uniform procedure across countries based on established frameworks • •

**International level**

- translation of the local findings and conclusions using a structured forward-backward procedure, supported by professional translators •

**Reporting**

- use of guidelines for reporting the synthesis of qualitative research<sup>80</sup> •

$t_1$ : time point 1= three to six months after start of the initial treatment for early rheumatoid arthritis;  $t_2$ : time point 2= at least one year after start of the initial treatment for early rheumatoid arthritis.

## **ETHICS AND DISSEMINATION**

### **Ethical considerations**

EQPERA will apply the principles established in the Declaration of Helsinki.<sup>61</sup> Participants will provide written informed consent before data collection of  $t_1$  and  $t_2$ . Only coded and interpreted data will be shared between the local teams for the meta-analysis. Ethics approval for the original studies were granted by the responsible institutional review boards.

### **Dissemination of results**

Every country will prepare a publication on their national findings. Two EQPERA main papers are foreseen: 1) the present paper describes the rationale, design and methods of EQPERA; 2) a publication on the results of the meta-analysis. Next to peer-reviewed publications, we will also disseminate our findings in (inter)national research presentations, and also patient organizations will be updated about the study findings.

## **CONCLUSION**

In EQPERA, the aim is to confirm the Belgian findings on patient-preferred outcomes in early RA in a European context, and provide a study protocol that has the potential to offer a methodological framework for further exploration of transferability in other contexts. Ultimately, study findings will be used to inform and optimize current care initiatives in early RA in order to address the unmet need of patient-centered care in RA.

## **ACKNOWLEDGEMENTS**

We wish to thank Patrick Verschueren and Bernadette Dierckx de Casterlé for sharing their methodological advises on the meta-analysis approach.

## **Author contributions**



1  
2  
3 KE and RW had the main idea of the study. KE, AB, AG, IL, EM, JV, RW and YH contributed  
4 to the design of the study. KE, YH and RW drafted the manuscript. KE, AB, AG, IL, EM, JV,  
5 RW and YH were involved in the editing of the manuscript. All authors read and approved the  
6 final version of the manuscript. Apart from the first and last author, the other authors are  
7 listed in alphabetical order.  
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### 14 **Funding statement**

15  
16 This work was supported by an unrestricted educational grant of Bristol-Myers Squibb, by a  
17 travel grant from Fonds voor Wetenschappelijk Reuma Onderzoek (fund for Scientific  
18 Rheumatism Research) (Belgium) and by Southern Health Care Region (Sweden).  
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### 24 **Competing interest statement**

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26 None declared.  
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### 31 **Patient consent**

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33 Will be obtained.  
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### 37 **Ethics approval**

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39 The Netherlands: the Medical Research Ethical Committee of Arnhem-Nijmegen waived  
40 ethical approval since the medical research involving human subjects act did not apply to this  
41 study; Sweden: ethical approval was obtained from the Regional Ethical Review Board at  
42 Lund University, Sweden; Belgium: ethical approval was obtained from the Human Research  
43 Ethics Committee of the University Hospitals Leuven.  
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### 51 **Data sharing statement**

52  
53 Not applicable.  
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30 **Figure 1** Overview of the European, longitudinal, multimethod qualitative research  
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32 design. *t*: time point.  
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36 **Figure 2** Forward-backward translation framework applied to translate the interview  
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38 questions and procedures.  
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42 **Figure 3:** Simplified outline of the used frameworks,<sup>25 45-48</sup> and the included steps in the  
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44 local analyses and the meta-analysis.  
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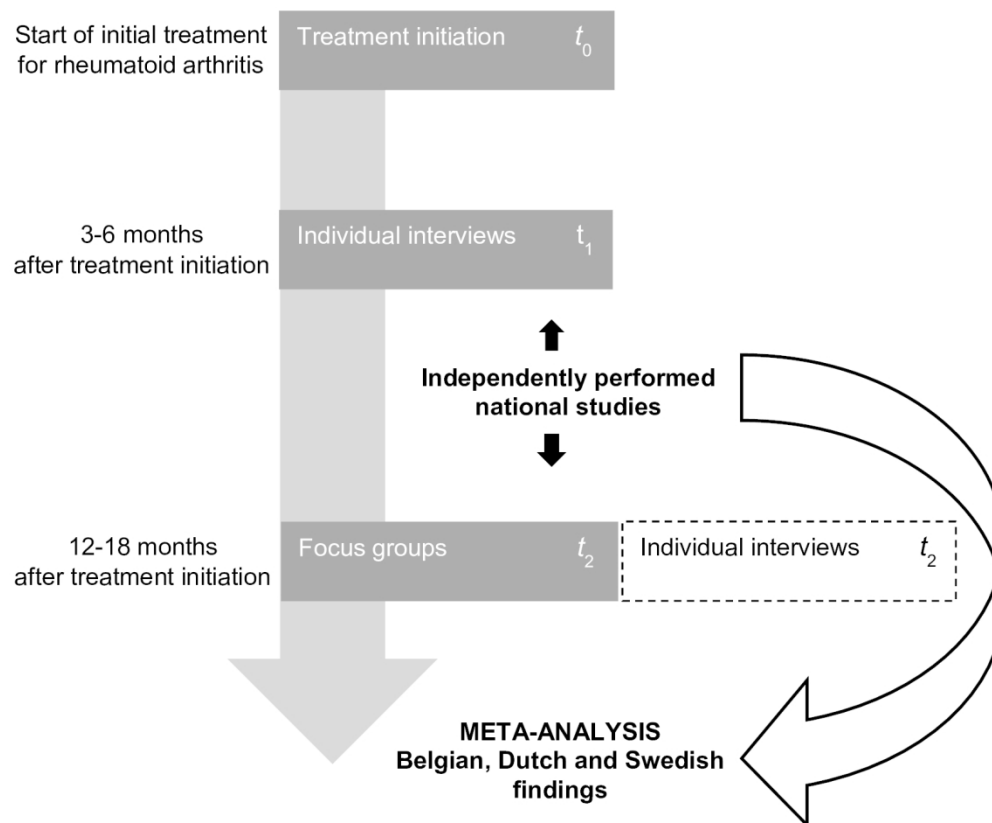


Figure 1 Overview of the European, longitudinal, multimethod qualitative research design. *t*: time point.

143x118mm (300 x 300 DPI)



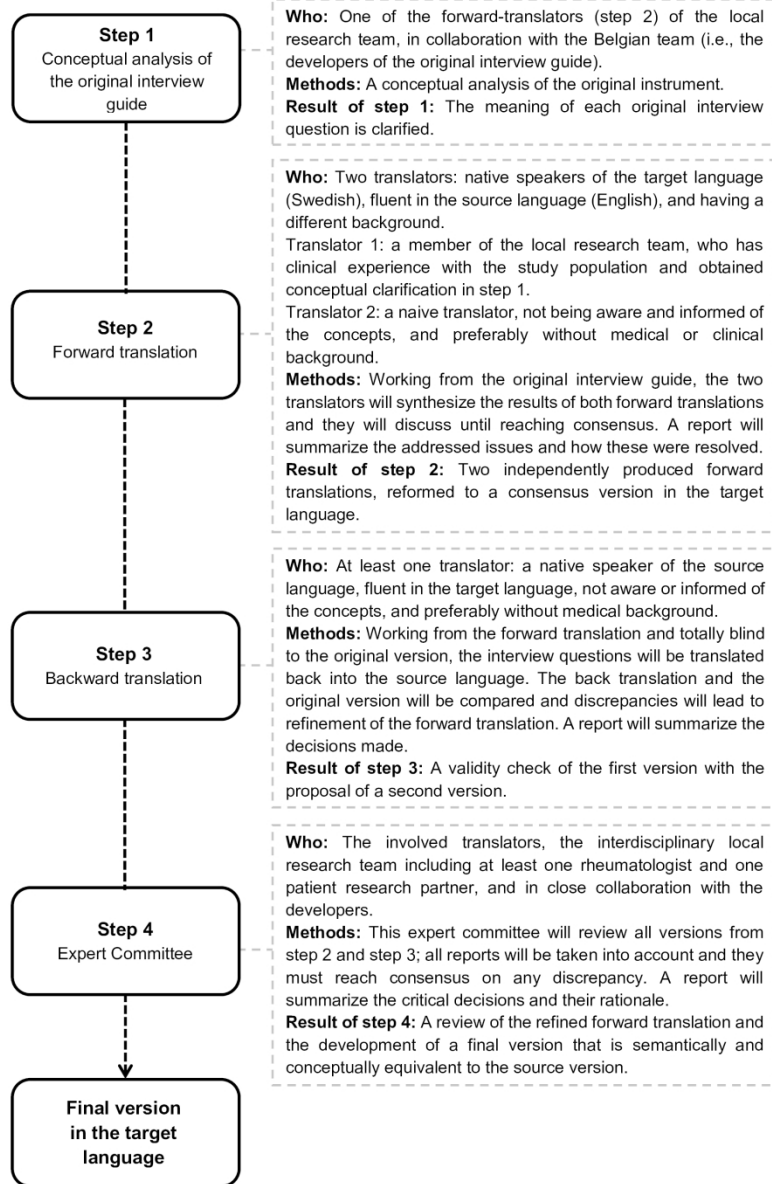


Figure 2 Forward-backward translation framework applied to translate the interview questions and procedures.

163x249mm (300 x 300 DPI)

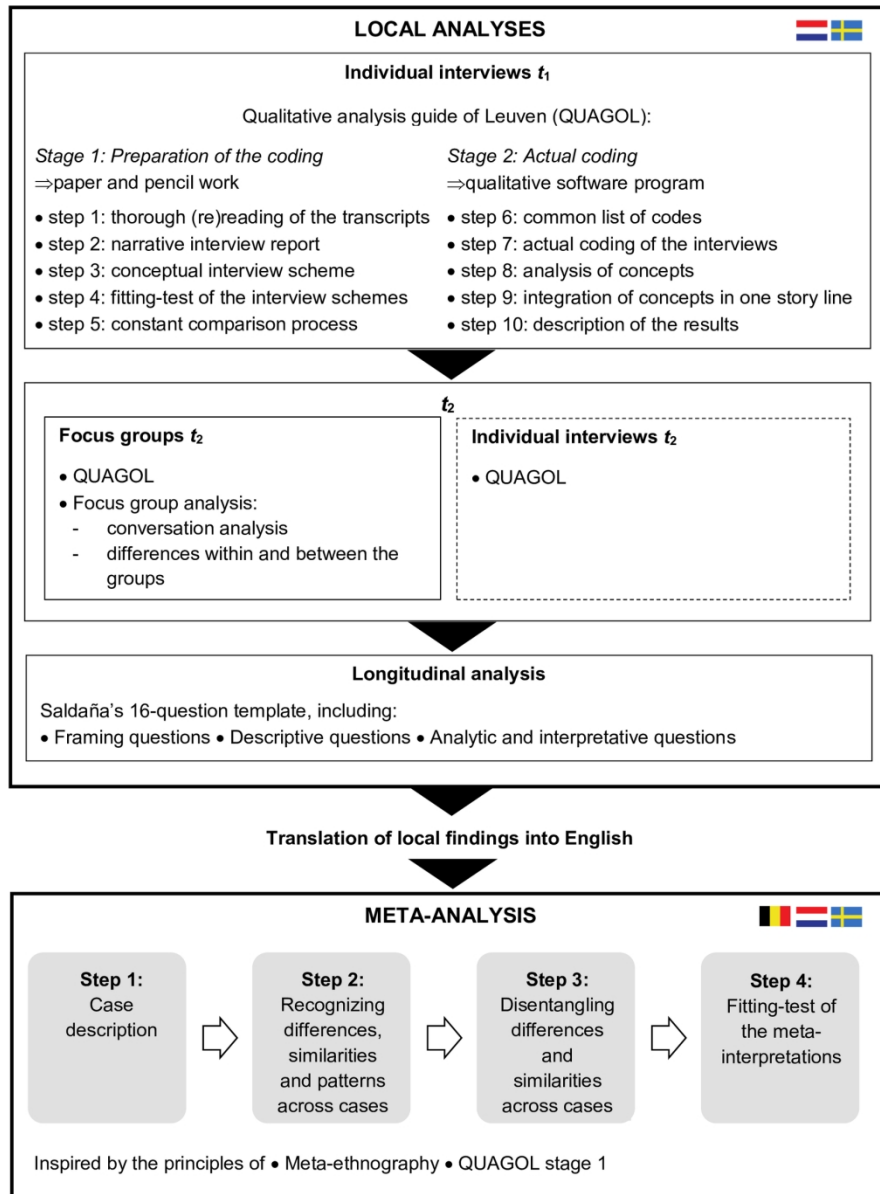


Figure 3: Simplified outline of the used frameworks,<sup>25 45-48</sup> and the included steps in the local analyses and the meta-analysis.

146x197mm (300 x 300 DPI)

**Supplementary file 1** Main interview questions and procedures for the individual interviews ( $t_1$  and  $t_2$ ) and focus groups ( $t_2$ ). Most aspects of the methods of  $t_1$  and  $t_2$  have been used in the study of Van der Elst et al.

<b>Individual interviews (<math>t_1</math> and <math>t_2</math>) and focus groups (<math>t_2</math>)</b>	<b>Context questions</b>
	<ul style="list-style-type: none"> <li>- What type of treatment are you currently receiving?</li> <li>- Have there been any changes in your treatment plan? If so, why and what type of changes?</li> </ul>
<b>Individual interviews at <math>t_1</math></b>	<b>Interview questions and procedures</b>
	<p><b>Preparatory phase (5 to 10 minutes)</b></p> <p>To set the scene for the interview, participants were asked to write down as many keywords as possible describing:</p> <ul style="list-style-type: none"> <li>- the impact of RA on their life</li> <li>- which outcomes of their illness and treatment they considered most important.</li> </ul>
	<p><b>Start of the interview</b></p> <p>The interviews began by discussing participants' written answers to those two questions. Participants were asked to elaborate on their keywords.</p> <ul style="list-style-type: none"> <li>- Can you tell me how RA affects your daily life?</li> <li>- Which outcomes of your illness and antirheumatic treatment are important to you at this moment?</li> </ul>
	<p><b>Proceeding of the interview</b></p> <p>The order of the other interview questions was determined by the participants' answers during the interview:</p> <ul style="list-style-type: none"> <li>- How has the treatment been working for you so far?</li> <li>- How do you decide whether or not your treatment is working?</li> <li>- What made you decide to start treatment?</li> <li>- What were your expectations of your antirheumatic treatment at the start of treatment?</li> <li>- To what extent do the expectations you had at the start of your treatment match your current expectations?</li> </ul>
	<p>*Three questions were added after the first interviews: Other patients talked about taking less medication*, returning to a normal life*, feeling better*. Is this something you recognize? What do you feel about that?</p>

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Probing questions: Could you tell me more about that? Could you give an example?

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**End of the individual interview:** Is there anything else you would like to add?

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## Focus groups at t<sub>2</sub>

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### Round 1: Preparatory phase (5 to 10 minutes)

The moderator introduced the phenomenon of interest, after which each group member was asked to independently prepare answers to the question below by writing down as many keywords as possible. Each answer was written on a separate Post-it®.

- Which outcomes of your illness and antirheumatic treatment are important to you at this moment?

Next, participants were asked to try to order their Post-its® on a vertical scale, from most important (top) to least important (bottom).

Participants were simultaneously asked to think about the following questions:

- What important treatment results have already been achieved?
  - At present, is there anything you would like to change or improve regarding your disease or treatment?
- 

### Round 2-step 1: Round-robin listing

All group members were asked to reveal and clarify, one by one, their personally preferred outcomes in order of importance. Meanwhile, the observer wrote these outcomes on a flipchart in front of the group.

- Who would like to share your personally valued outcomes with the group, in order of importance?
  - Could you please clarify why these outcomes of your disease and antirheumatic treatment are important to you?
  - Why did you designate that specific outcome to be the most important?
  - Is there anything else you would like to add?
- 

### Round 2-step 2: Developing a group list of patient-preferred outcomes

The group was asked to generate a consensus list by reviewing and merging all recorded outcomes and agreeing on the name and properties of each outcome on the list.

- Could any of the individual expectations be grouped?
  - Who would like to suggest a name and meaning for this outcome?
-

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3 - Do you think all the important outcomes are mentioned on the  
4 group list? Is there anything else you would like to add?

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5  
6 **Round 2-step 3: Eliciting personal preferred outcomes**

7 Starting from the consensus list of patient-preferred outcomes that  
8 resulted in step 2, each group member was asked to independently try  
9 to select his or her five top outcomes from this list, using the Post-it®  
10 ordering scheme.  
11

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12 **Round 2-step 4: Eliciting preferred outcomes in the actual stage of**  
13 **RA**

14 The group was then asked to discuss a collective top 5 outcomes and to  
15 consider influencing factors.

- 16  
17 - Looking at the group list, what outcome would you order as most  
18 important?  
19 - What outcome would you order second...fifth?  
20 - Can you tell us why this outcome is either important to you or  
21 not?  
22  
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24 **End of round 2:** That is it for the second round. Is there anything else  
25 to add?  
26

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27 **Round 3: Exploring the view of participants on the evolution of their**  
28 **patient-preferred outcomes over the past year**

29 The focus groups ended by exploring the participants' views on potential  
30 changes in personally preferred outcomes over time: During the  
31 individual interview of last year, you were asked for your preferred illness  
32 and treatment outcomes. In the meantime, you have gained more  
33 experience with your disease and treatment and the critical disease  
34 stage has passed.  
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- 38 - Do you feel that other results are now more important to you  
39 than the ones you identified at the start or during your interview  
40 last year?  
41 - Could you explain why this has or has not changed?  
42 - Are there outcomes that are now more, less or no longer  
43 important to you?  
44 - Why do you think that these are now more or less, or no longer  
45 important than a year ago, or are no longer important? What  
46 may have caused this change in importance?  
47 - Do you have an example of an outcome that has changed in  
48 importance compared to that outcome in the early disease  
49 stage? Why do you think this has changed? Could you clarify  
50 this in more detail?  
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3 - In general you mention (more or less) similar/different outcomes  
4 of importance compared to last year (in the early disease stage).  
5 What is your opinion on this observation?  
6

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7 **End of round 3:** This is the end of the third round. Is there anything else  
8 to add?  
9

---

10 Probing sub-questions: Is this outcome also important or not important  
11 to other group members? Are there any suggestions from other group  
12 members? Is there anyone who has a different opinion on the matter?  
13 Is it difficult for you to share your opinion on this? Who agrees or  
14 disagrees and why? Does everyone agree? Who would like to add  
15 something?  
16  
17

---

18 **End of the focus group**

- 19 - What is your general conclusion about today's focus group on  
20 preferred and important outcomes of disease and treatment in  
21 the actual disease stage?  
22  
23 - To summarize, you talked about [...].  
24  
25 - Do you agree with this summary of today's focus group?  
26

---

26 **Individual**  
27 **interviews at  $t_2$**   
28

---

29 **Preparatory phase (5 to 10 minutes)**

30 Please, consider the next 5 to 10 minutes the question below by writing  
31 down as many keywords as possible. The interviews will begin by  
32 discussing your written answers to this question:  
33

- 34 - Which outcomes of your illness and antirheumatic treatment are  
35 important to you at this moment?  
36

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37 **Start of the interview**

- 38 - Can you tell me what you have written down? So, which  
39 outcomes of your illness and antirheumatic treatment are  
40 important to you at this moment?  
41  
42

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43 **Proceeding of the interview**

44 **Exploring patient-preferred outcomes**

- 45 - How has the treatment been working for you so far?  
46  
47 - To what extent do the expectations you had at the start of your  
48 treatment match your current expectations?  
49

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50 **Exploring the view of participants on the evolution of their**  
51 **preferred outcomes over the past year**

52 Last year, during the interview, you mentioned that the following  
53 outcomes of your treatment were important: ..... ( $t_1$  keywords of  
54 the  $t_2$  participant).  
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3 - Do you feel that other results are now more important to you  
4 than the ones you identified at the start or during your interview  
5 last year? Could you explain why this has or has not changed?  
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7 - Are there outcomes that are now more, less or no longer  
8 important to you?  
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10 - Why do you think that these are now more or less, or no longer  
11 important than a year ago, or are no longer important? What  
12 may have caused this change in importance?  
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14 - Do you have an example of an outcome that has changed in  
15 importance compared to that outcome in the early disease  
16 stage? Why do you think this has changed? Could you clarify  
17 this in more detail?  
18

---

19 **Patient-preferred outcomes compared to the focus groups at  $t_2$**

20 During the focus groups the following 5 treatment outcomes were found  
21 to be most important: 1) preferred outcome; 2) preferred outcome; 3)  
22 preferred outcome; 4) preferred outcome; 5) preferred outcomes.

- 23  
24 - I wonder if you recognize yourself in this? Could you explain why  
25 this is or is not the case?  
26

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27 **End of the individual interview:** Is there anything else you would like  
28 to add?  
29

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30  $t_1$ : time point 1= three to six months after start of the initial treatment for early rheumatoid arthritis.

31  $t_2$ : time point 2= at least one year after start of the initial treatment for early rheumatoid arthritis.

32 Van der Elst K, Meyfroidt S, De Cock D, et al. Unraveling Patient-Preferred Health and Treatment  
33 Outcomes in Early Rheumatoid Arthritis: A Longitudinal Qualitative Study. *Arthritis Care Res (Hoboken)*  
34 2016;68(9):1278-87.  
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## Supplementary file 2 EQPERA data quality assurance reporting tool

Domain 1: Research team and reflexivity	
Item	Guide questions/description
<b>Researcher characteristics</b>	
1. Interviewer/moderator/observer	Who conducted the interviews/ focus groups? (who observed the focus groups?) <i>Maximum 2 interviewers at t<sub>1</sub> and t<sub>2</sub> /country and maximum 1 moderator at t<sub>2</sub>/country; preferably the same observer(s) for each focus group</i>
2. Credentials / background	What were the researcher's credentials? (e.g., PhD, RN)
3. Occupation	What were the researcher's occupation at the time of the study?
4. Gender	Was the researcher male or female?
5. Experience and training	What experience or training did the researcher have?
<b>Relationship with participants</b>	
6. Relationship established	Was a relationship established prior to study commencements? (e.g., health professional)
7. Participant knowledge of the interviewer	What did the participant know about the researcher? (e.g., personal goals, reasons for doing the research)
8. Interviewer characteristics	What characteristics were reported about the interviewer/moderator/observer? (e.g., bias, assumptions, reasons and interest in the research topic)
Domain 2: Study design (a longitudinal, qualitative, explorative study)	
<b>Participant selection</b>	
9. Sampling	<ul style="list-style-type: none"> <li>- How were participants selected (purposive)</li> <li>- Mono or multicenter sampling?</li> <li>- Type of recruitment center(s)? (i.e., academic hospital, general hospital or private practice?)</li> </ul>
10. Method of approach	<ul style="list-style-type: none"> <li>- Who invited the participants?</li> <li>- How were participants approached? (e.g., face to face, telephone, mail, email)</li> </ul>
11. Sample size	<p>How many participants were in the study?</p> <ul style="list-style-type: none"> <li>- at t<sub>1</sub>: number of individual interviews</li> <li>- at t<sub>2</sub>: number of participants per focus group / number of individual interviews</li> </ul>



12. Non-participation	<ul style="list-style-type: none"> <li>- How many eligible patients could potentially be recruited?</li> <li>- How many people were approached and how many of them refused to participate or dropped out?</li> <li>- Reasons? (if shared) <ul style="list-style-type: none"> <li>o Not interested in participation (refusal)</li> <li>o Drop out (type 1): in case <math>t_1</math> interview was scheduled and cancelled</li> <li>o Not interested in participation at <math>t_2</math> (drop out, type 2)</li> <li>o Not interested in participation in a focus group, but willing to participate in an individual interview instead at <math>t_2</math></li> <li>o Drop out (type 3): in case <math>t_2</math> interview was scheduled and cancelled</li> </ul> </li> </ul>
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**Setting**

13. Setting of data collection	Where was the data collected?
14. Presence of non-participants	Was anyone else present besides the participant and researchers?
15. Description of sample	What are the important characteristics of the sample? (e.g., demographic data)

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**Data collection**

16. Interview guide	<ul style="list-style-type: none"> <li>- Were questions, prompts, guides provided by the authors?</li> <li>- Was the interview guide pilot tested?</li> <li>- Is it being made available?</li> </ul>
17. Focus group guide	<ul style="list-style-type: none"> <li>- Were questions, prompts, guides provided by the authors?</li> <li>- Was the interview guide pilot tested?</li> <li>- Is it being made available?</li> </ul>
18. Audio / visual recording	Did the research use audio or visual recording to collect the data?
19. Data collection method	<ul style="list-style-type: none"> <li>- How were the data collected? (<math>t_2</math>: focus group or individual interview?)</li> <li>- Were repeat interviews carried out at <math>t_2</math>?</li> </ul>
20. Field notes	<ul style="list-style-type: none"> <li>- Were field notes made during and/ or after the interview or focus group? <math>\Rightarrow</math> if yes, please record them in the descriptive or methodological interview report.</li> </ul>

	- Were short reports prepared after each interview?
21. Duration	What was the duration of the interviews or focus groups?
22. Data saturation	- Was data saturation discussed? - After how many interviews was data saturation reached? ( <i>Definition in EQPERA: "if the last 3 interviews do not provide new information, insights or additional understanding to accomplish the study aims"</i> )

### Domain 3: Analysis and findings

#### Data analysis

23. Number of data coders	- How many data coders coded the data? - Who coded the data?
24. Independent coding	Was the analysis repeated by more than one researcher to ensure reliability?
25. Data analysis method	How were themes and concepts identified from the data? ( <i>e.g., Were themes identified in advance (framework-based) or derived from the data (data-driven)?</i> )
26. Patient research partners	Did patient research partners provide feedback on the findings, and in which part(s) of the data analysis were they involved?
27. Software	What software was used to manage the data?

#### Reporting

28. Quotations presented	- Were participant quotations presented to illustrate the themes/findings? - Was each quote identified? ( <i>e.g., participant number, gender, age</i> )
29. Data and findings consistent	Was there consistency between the data presented and the findings?
30. Clarity of themes	Were themes clearly presented in the findings?

### Domain 4: Data management strategies

#### Data recording

31. Recording changes and decisions	Were changes to the interview guide, the evolution in themes, deviations from the research protocol, and major local project decisions carefully documented along with the rationale for change? <i>⇒ to recall decisions</i> <i>⇒ the use of a research log book is recommended</i>
-------------------------------------	--

32. Recording interview data	Did you record the data with at least 2 audio recorders? ⇒ <i>to prevent missing data</i>
<b>Data storing</b>	
33. Routinely storing of data	Was the data (e.g., audio files, transcripts, interview reports and field notes, patient-reported and clinical data, informed consents) or the project database routinely submitted to a central data repository or a secured cloud storage system? ⇒ <i>to avoid missing data and to easily manage large amounts of data like in qualitative research</i> ⇒ <i>a uniform transcript header and file name could facilitate data storing (e.g., T1.number of interview.ddmmyyyy.initials of interviewer)</i>
<b>Data check</b>	
34. Internal audit	Could the evidence (field notes, interview transcripts, recordings, reasons for interview guide adaptations,...) be inspected by others?
35. Preventing missing data	Did the principal investigator routinely check for missing data?
<b>Data collection</b>	
36. Recruitment flow	Was the recruitment flow carefully documented? ⇒ <i>the use a research log book (enrollment spread sheet) is suggested</i>
37. Templates	Did you check the data collection templates and the Excel spread sheet?
38. Local interview guide	Translation/cultural adaptation interview guide: <ul style="list-style-type: none"> <li>○ Did you use the proposed framework to translate the interview guide into the source language?</li> <li>○ Were cultural adaptations needed? ⇒ <i>please record these in your research log book, together with the timing and the reason for adjustment</i></li> </ul>
39. Avoiding and handling the presence of a third person	⇒ <i>focus of attention during interview scheduling: Was the purpose of a one to one interview mentioned to the participant?</i> ⇒ <i>if someone else was present, did this affect the interview/data collection? Please reflect on this in the descriptive interview report.</i>

1 2 3 4 5 6 7 8 9 10 11 12 13 14	40. Introducing the interview	Did you prepare and practice the interview introduction? ⇒ <i>to maximize the interview return</i> ⇒ <i>key words: welcoming the participant; introducing yourself; clarifying the purpose and importance of research, the importance of participant contribution, expectations regarding the participant (e.g., no good or wrong answers), role of the interviewer/moderator/observer, (t<sub>2</sub>: "rules" regarding group discussion), ethical aspects; "Any questions?"; mobile phone on silent mode)</i>
15 16 17 18 19	41. Interview burden	It is recommended to conduct 1 individual interview/day, with a maximum of 2 interviews/day ⇒ <i>to avoid interview burden and to have sufficient time to reflect on each interview</i>
20 21 22 23 24	42. Interview reports	Did you write for each interview/focus group 3 short reports? ( <i>i.e., content report, descriptive report, methodological report</i> )
25 26 27 28	43. Iterative process	Did you use an iterative process of data collection and analysis? ⇒ <i>to support data saturation</i>
29	<b>Data analysis</b>	
30 31 32 33 34 35	44. Analysis guide	Did you use Qualitative Analysis Guide of Leuven (QUAGOL) to guide your data analysis? Did you use Saldaña's guiding questions for analyzing the longitudinal data)
36 37 38 39 40 41 42 43 44 45 46	45. Peer debriefings	Were regular peer debriefings held? ⇒ <i>time for reflection (in team): to discuss the interview return, the development of new themes and to question and confirm saturation of themes</i> ⇒ <i>early in de coding and interviewing process, more frequent meetings are suggested</i> ⇒ <i>please make a short report of each debriefing to recall discussions</i>
47 48 49	46. Team analysis	Was looked at the data in team (from different perspectives looking at the data)
50	<b>Transcription</b>	
51 52 53 54 55 56 57	47. Transcription guidelines	Who transcribed the data? ⇒ <i>&gt;1 person: did you apply a uniform transcription method? (e.g., agreements about the level of details, to obtain confidentially, to reproduce the exact words spoken)</i>

⇒ *external transcriber: was the interview transcript reviewed by the interviewer on data quality and accuracy of transcribing? How did you approach this quality check?*

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**Team approach**

48. Patient research partners

What was the exact role of the patient research partners in the study

49. Interdisciplinary team

Who joined the interdisciplinary team, and what was their contribution?

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**Initiation session**

50. Project initiation

Did the local research team (at least the principal investigator) followed the initiation session lead by the project leader at  $t_1$  and at  $t_2$ ?

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peer review only

# BMJ Open

## European Qualitative research project on Patient-preferred outcomes in Early Rheumatoid Arthritis (EQPERA): rationale, design and methods of a multinational, multicenter, multilingual, longitudinal qualitative study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-023606.R1
Article Type:	Protocol
Date Submitted by the Author:	08-Oct-2018
Complete List of Authors:	<p>Van der Elst, Kristien; University Hospitals Leuven, Department of Rheumatology; KU Leuven–University of Leuven, Skeletal Biology and Engineering Research Center, Department of Development and Regeneration</p> <p>Bremander, Ann; Lund University, Department of Clinical Sciences, Section of Rheumatology; Spenshult Research and Development Center</p> <p>De Groef, An; KU Leuven – University of Leuven, Department of Rehabilitation Sciences; University Hospitals Leuven, Department of Physical Medicine and Rehabilitation</p> <p>Larsson, Ingrid; Halmstad University, School of Health and Welfare, ; Spenshult Research and Development Centre,</p> <p>Mathijssen, Elke; Sint Maartenskliniek, Department of Rheumatology</p> <p>Vriezekolk, J; Sint Maartenskliniek</p> <p>Westhovens, Rene; University Hospitals Leuven, Department of Rheumatology; KU Leuven–University of Leuven, Skeletal Biology and Engineering Research Center, Department of Development and Regeneration</p> <p>van Eijk-Hustings, Yvonne; Maastricht University Medical Center, Department of Clinical Epidemiology and Medical Technology Assessment; Maastricht University Medical Center, Department of Rheumatology</p>
<b>Primary Subject Heading</b>:	Research methods
Secondary Subject Heading:	Qualitative research
Keywords:	Rheumatoid Arthritis, QUALITATIVE RESEARCH, Longitudinal study, Patient Preference

SCHOLARONE™  
Manuscripts

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3 **European Qualitative research project on Patient-preferred outcomes in Early**  
4 **Rheumatoid Arthritis (EQPERA): rationale, design and methods of a**  
5 **multinational, multicenter, multilingual, longitudinal qualitative study**  
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8  
9 Kristien Van der Elst<sup>1,2</sup>, Ann Bremander<sup>3,4,5</sup>, An De Groef<sup>6,7</sup>, Ingrid Larsson<sup>5,8</sup>, Elke  
10 Mathijssen<sup>9</sup>, Johanna Vriesevink<sup>9</sup>, René Westhovens<sup>1,2</sup>, Yvonne van Eijk-Hustings<sup>10,11</sup>  
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## ABSTRACT

**Introduction:** Including the patient perspective is important to achieve optimal outcomes in the treatment of rheumatoid arthritis (RA). Ample qualitative studies exist on patient outcomes in RA. A Belgian study recently unraveled what matters most to patients throughout the overwhelming and rapidly evolving early stage of RA. The present study, European Qualitative research project on Patient-preferred outcomes in Early Rheumatoid Arthritis (EQPERA) was created to contribute to a more universal understanding of patient-preferred health and treatment outcomes by integrating the perspectives of patients with early RA from three European countries.

**Methods and analysis:** In EQPERA, a qualitative, explorative, longitudinal study will be implemented in The Netherlands and Sweden, parallel to the methods applied in the previously conducted Belgian study. In each country, a purposive sample of patients with early RA will be individually interviewed 3-6 months after start of the initial RA treatment and subsequently, the same participants will be invited to take part in a focus group 12-18 months after RA treatment initiation. Data collection and analysis will be independently conducted by the local research teams in their native language. A meta-analysis of the local findings will be performed to explore and describe similarities, differences and patterns across countries.

**Ethics and dissemination:** Ethics approval was granted by the responsible local ethics committees. EQPERA follows the recommendations of the Declaration of Helsinki. Two main papers are foreseen (apart from the data reporting on the local findings) for peer-reviewed publication.

**Key words:** Rheumatoid Arthritis, Qualitative research, Longitudinal study, Patient Preference



## STRENGTHS AND LIMITATIONS OF THIS STUDY

- The specific nature of the study, in which qualitative studies are carried out in different countries and languages using a uniform methodology, is novel, and we report in a transparent way about our approach and challenges.
- As no formal meta-analysis method was present in literature applicable to our study, we developed a method based on established techniques for the synthesis of qualitative research, which can guide other researchers interested in conducting this type of research.
- Several quality enhancing strategies are applied to yield sound results in this multinational, multilingual, longitudinal qualitative study.
- The participating countries might have rather similar cultural views and healthcare systems, which would strengthen the Belgian findings, however, the study protocol offers a methodological framework for research in different parts of the world.

## INTRODUCTION

In rheumatoid arthritis (RA), the outcome landscape dramatically changed over the past decades. RA is the most prevalent chronic, auto-immune inflammatory joint disease. It was typically described as an inevitably progressive disease with a destructive and disabling natural course. The continuous growth in effective pharmacological treatments contributed to this change, but the introduction of early therapy was one of the main drivers of transformed health outcomes of patients with RA.<sup>1</sup> Nowadays, remission or at least low disease activity have become realistic treatment targets for a notable proportion of the population.<sup>2</sup>

Nevertheless, the burden of disease and unmet needs remain considerable.<sup>3 4</sup> For example, most of the patients are at working age upon diagnosis, but work disability rates remain high.<sup>5</sup> Furthermore, patients with RA indicated the need for greater emotional support, and greater psychological support to manage the impact of disease on domains such as pain, fatigue, work and leisure.<sup>6 7</sup> Hence, it seems that patient preferences are not sufficiently understood and met by health professionals. In a recent report, patient-centered care was identified as a recurrent unmet need across rheumatic diseases, including RA.<sup>8</sup> Patient-centered care can be translated as care that is guided by the values and preferences of the patients,<sup>9</sup> with patient preferences referring to the perspective, beliefs and expectations of patients regarding their health and life.<sup>10</sup> As patient-centeredness is acknowledged as one of the key dimensions of high-quality care,<sup>11</sup> integrating the patient perspective in outcome assessment is increasingly advocated to achieve optimal outcomes in the treatment of RA.<sup>12</sup>

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Qualitative studies shed light on the different views that patients with RA have on outcome compared to health professionals. These studies revealed the importance of fatigue and independence, among others,<sup>14-16</sup> to consider in daily practice on top of the traditional measures of disease activity, i.e., the swelling of joints and laboratory parameters of inflammation. Remarkably, limited attention has been given to the perspective of recently

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3 diagnosed patients. The early disease stage is probably the most daunting period for  
4 patients, indicating specific needs and preferences.<sup>17 18</sup> The Belgian qualitative study of Van  
5 der Elst et al. provided new insights into patient-preferred outcomes in early RA, concluding  
6 that returning to 'normality' as soon as possible was the core preferred outcome, which  
7 related to aspects of disease control and participation, physical and mental aspects.<sup>19</sup>  
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9 However, understanding is lacking about the transferability of these local findings to other  
10 settings and cultures.  
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18 Despite recommendations for RA management, literature shows that there are differences in  
19 how rheumatology services are viewed and practiced across countries.<sup>20 21</sup> These differences  
20 may be attributable to characteristics of the national healthcare systems, local customs,  
21 practices and values. Such cultural differences may consequently influence how patients  
22 evaluate their disease. For example, the survey study of Van Tuyl et al. demonstrated that  
23 the country in which patients were sampled resulted in slightly different key domains on how  
24 they perceived remission of disease.<sup>22</sup> Hifinger et al. showed that country of residence had  
25 an important influence on how patients with RA experienced fatigue.<sup>23</sup> It can thus be  
26 questioned whether patients in other countries would bring out other preferred outcomes.  
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38 To examine the transferability of the Belgian findings and to contribute to a more universal  
39 understanding of patient-preferred outcomes, we initiated the EQPERA consortium.  
40 EQPERA is the acronym for European Qualitative research project on Patient-preferred  
41 outcomes in Early Rheumatoid Arthritis. It is a multicenter, multilingual, longitudinal  
42 qualitative study across Belgium, The Netherlands and Sweden. The present paper reports  
43 about the international study protocol, based on the Belgian study procedures.  
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## 52 Objectives

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3 The overall research objective in EQPERA is to explore how local context influences patient-  
4 preferred health and treatment outcomes throughout the early disease course by integrating  
5 the perspectives of patients with early RA from three European countries.  
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8 The objective is twofold:  
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- 10 (i) to describe patient-preferred outcomes in early RA and how they change  
11 throughout the early disease course (national objective);  
12  
13 (ii) to identify differences, similarities and patterns in patient-preferred outcomes  
14 across the three European countries (international objective).  
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## 20 **METHODS AND ANALYSIS**

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22 The Belgian study was conducted during 2012-2013.<sup>19</sup> Based on the lessons learned and  
23 after multiple discussion rounds with the EQPERA steering group, an improved research  
24 protocol was written with the aim to implement a protocol as similar as possible in the other  
25 countries. Start of patient inclusion was 2016 in The Netherlands and 2017 in Sweden. We  
26 intend to publish the final results by the end of 2019.  
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### 35 **Study design**

36 A qualitative, explorative, longitudinal research design will be applied within a European  
37 context. As we study a research domain still lacking evidence, the use of qualitative methods  
38 is justified because we will learn from the rich descriptions of participants being shaped in  
39 their local contexts.<sup>24 25</sup> Longitudinal designs are relevant for studying complex phenomena  
40 and are specifically applicable in the context of a recent diagnosis since patients' perceptions  
41 and expectations may change during the overwhelming and rapidly evolving early disease  
42 stage. Previous research also suggests that the way patients experience and evaluate their  
43 disease can differ depending on disease duration.<sup>15 26 27</sup>  
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3 Patients with early RA will be invited to participate at two time points (Figure 1). At  $t_1$ ,  
4 participants will be individually interviewed 3-6 months after they have started their initial  
5 treatment for RA. At  $t_2$ , participants will be invited to take part in a focus group 12-18 months  
6 after RA treatment initiation. To address a potential dropout of participants at  $t_2$ , those who  
7 decline to participate in a focus group will be invited for a repeated individual interview  
8 instead. However, the preferred interview method at  $t_2$  remains the focus group method to  
9 align with the original design of the Belgian study.  
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18 The reason for selecting different interview methods at  $t_1$  and  $t_2$  is based on the input of  
19 patient research partners and aims to match with patient preference in the context of a recent  
20 diagnosis. At  $t_1$ , the individual interview method is chosen because adjusting to a recent  
21 diagnosis can be seen as a primarily individual matter. Consequently, sharing personal  
22 experiences and opinions in a group setting can be too confronting at that stage of disease.  
23 A timeframe of 3-6 months after initiation of the initial RA treatment is chosen to not interfere  
24 with the diagnostic and therapeutic procedures, however, still including patients' earliest  
25 views on preferred outcomes. Furthermore, it is assumed that a few months of experience  
26 with the disease and treatment would help patients to communicate more easily about their  
27 outcome preferences.  
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40 At  $t_2$ , focus groups are chosen above the individual interview method for two reasons. Firstly,  
41 compared to the first interview moment, participants may probably feel more comfortable in a  
42 group setting, because of a grown disease perspective and the potential interaction with  
43 other patients (e.g., in the waiting room) by then. Secondly, group interactions potentially  
44 help participants to remember significant events and bring out personal thoughts, which in  
45 turn may result in more and diverse data.<sup>25 28</sup> It is reasoned that after 12-18 months of  
46 treatment experience, participants have had sufficient time to develop their view on the  
47 disease, with perhaps an observable change in their preferences accordingly.  
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## Research context

EQPERA involves three countries in Northwest Europe: Belgium, The Netherlands and Sweden. These countries have a comparable organized healthcare system including a comprehensive social security system, however, differences exist in for example their reimbursement and referral system.

Participants will receive usual care according to local standards. Across countries, a comparable early RA management is implemented in respect of current international guidelines:<sup>29 30</sup> patients should be treated (i) early: as soon as the diagnosis is made; (ii) intensively, with methotrexate in the first treatment if possible; (iii) to target: treatment adjustments according to a predefined target of sustained remission or low disease activity. In addition, there is a common culture across the countries regarding interdisciplinary team care as key in disease management, but diversity can be expected concerning implementation aspects. For example, it has been shown that there is a wide variation in the role of nurses in the management of patients with chronic inflammatory arthritis<sup>20</sup>, and in the composition of rheumatology multidisciplinary teams.<sup>31</sup>

In each country, an early RA cohort is available, the local teams include experienced qualitative researchers with a good command of the English language, and funding possibilities are available to work out their national project. The EQPERA steering group consists of team members with different disciplinary backgrounds: nurses (KE, IL, EM, YH), physiotherapists (AB, AG), a psychologist (JV), a patient representative (AG) and a rheumatologist (RW).

## Level of collaboration between countries

Individual projects will be conducted in each country. The studies in Sweden and The Netherlands will be led by the local principal investigator (IL and EM, respectively) and

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2 supervised by the EQPERA project leader (KE), who designed and completed the Belgian  
3 qualitative study.<sup>19</sup>  
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9 Considering qualitative studies, potential language issues can be approached in two ways:  
10 either translate the transcripts and do the analysis in one place, or have the analysis done at  
11 each location and combine the data afterwards. After consideration, the project team decided  
12 that (i) data will be collected in the local settings by the local teams in their native language;  
13  
14 (ii) interviews will be transcribed in the original language and the transcripts will be analyzed  
15 by the local teams; (iii) only the results of the local analysis (i.e., interpreted data) will be  
16 combined for EQPERA purposes, and this after ending the analysis procedures and writing  
17 up the findings and conclusions in every country.  
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26 Original data will thus not be reviewed by the other teams (Figure 1). Centralizing data would  
27 mean translation of local transcripts to the common language in EQPERA (English).  
28 Translation holds the risk of losing the real meaning of words,<sup>32</sup> and would be expensive and  
29 time consuming because of the mountains of words that will be produced in every country.  
30 Above and beyond translation issues, we assumed that local data should ideally be analyzed  
31 by the people who are familiar with the local culture and context in order to get the most  
32 appropriate interpretations.  
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### 42 **Collaboration with patient research partners**

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44 As EQPERA aims to capture the patient perspective, the project would benefit from active  
45 collaboration with patient representatives, or those who have the lived experience of RA.  
46 Following the recommendations of the European League Against Rheumatism for the  
47 inclusion of patient representatives in scientific projects,<sup>33</sup> each local team will preferably  
48 collaborate with two patient research partners.  
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3 The local principal investigators will be responsible for coordinating this research  
4 partnership, being guided by the FIRST (i.e., Facilitate, Identify, Respect, Support and Train)  
5 framework of Hewlett and colleagues.<sup>34</sup> The exact level of the patient researchers'  
6 contribution will depend on local agreements (feasibility). In general, they will help by  
7 reflecting on the methods, formulating clear and understandable interview questions,  
8 interpreting and explaining data, and providing feedback on the readability of the patient  
9 information leaflet and informed consent form.  
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## 18 **Participants**

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20 Eligible patients will have to meet the following inclusion criteria: (i) confirmed diagnosis of  
21 RA, in accordance with the American College of Rheumatology/European League Against  
22 Rheumatism 2010 criteria;<sup>35</sup> (ii) time between diagnosis and start of RA treatment of less or  
23 equal than 1 year; (iii) minimum age of 18 years; (iv) speak, read and write the local  
24 language; (v) started the initial RA treatment 3-6 months ago.  
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## 32 **Sampling**

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34 Every country will strive to include a broad range of perspectives in their sample. To ensure  
35 this variation, participants will be purposively sampled based on their (i) age/life phase; (ii)  
36 gender; and (iii) treatment progress/treatment experience. Moreover, every country will apply  
37 a multicenter recruitment to account for possible variation in region.  
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45 Sampling in qualitative research corresponds to the assumption that collected data is of  
46 sufficient depth, i.e., representing the various views and opinions of the population with no  
47 added value of including more participants for answering the research question.<sup>36 37</sup> As there  
48 is no standardized definition of data saturation, we decided that data collection can be  
49 stopped if three consecutive interviews do not result in new themes or additional  
50 understanding (local team decision).  
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5 At  $t_1$ , we estimate that around 20 participants in every country will be needed to reach data  
6 saturation. At  $t_2$ , the sample sizes will foremost depend on the interest and willingness of  
7 participants to participate again. We aim for 4-8 participants in each focus group, which  
8 seems an appropriate number to keep the discussions manageable and stimulate  
9 contribution of every group member.<sup>36 38</sup> If possible, patient characteristics will be taken into  
10 account to create a mix of perspectives in the groups.  
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## 18 **Recruitment**

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20 In each country, patients are recruited from multiple centers across different geographic  
21 locations, including academic and non-academic rheumatology centers. In Belgium, patients  
22 were sampled from nine centers across Flanders. The participating centers in The  
23 Netherlands are located in Nijmegen and Woerden, and in Sweden these are located in  
24 Lund, Malmö and Halmstad. A recruitment template will help the local teams to consider the  
25 main variables for creating heterogeneity in their samples.  
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## 35 **Data collection**

### 36 **The interview guides**

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38 The semi-structured interview guides include pre-defined topics, with open-ended questions,  
39 and probing questions to reach a higher level of detail. All questions relate to the central  
40 interview question: 'Which outcomes of your illness and antirheumatic treatment are  
41 important to you at this moment?'. In every country, the interview guides will have the same  
42 content at start, and main questions will be fixed across countries. Data collection and  
43 analysis will be performed simultaneously, making it possible to adapt the interview guides if  
44 necessary to increase participants' understanding or to reach data saturation (local team  
45 decision). If adaptations are needed, these will be documented in the local research journal.  
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3 The content of the interview guides is inspired by previous qualitative studies on outcomes  
4 from the patient perspective.<sup>14 16 39</sup> In EQPERA, Dutch and Swedish versions of the Belgian  
5 interview guides (Flemish language) will be prepared by the local teams. Given similarities  
6 between the Flemish and Dutch language, minor adaptations will be applied after discussion  
7 and consensus with the Belgian team. Forward and backward translation will be used to  
8 prepare translations to English and Swedish (Figure 2).<sup>40 41</sup> The main interview questions and  
9 the interview procedures are elucidated in Supplementary file 1.  
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### 18 Individual interviews ( $t_1$ )

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20 At  $t_1$ , individual, face-to-face interviews will be conducted by maximum 2 interviewers per  
21 country, who are not involved in participants' clinical care. As the patient research partners  
22 noted that patients are in general not used to talk about outcome preferences, they will be  
23 asked to prepare written key words regarding the central interview question. The interviewer  
24 will start by elaborating on these key words. It is anticipated that interviews will last no longer  
25 than 60 minutes.  
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### 34 Focus groups ( $t_2$ )

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36 Focus groups will be facilitated by one of the interviewers of  $t_1$  in assistance of at least one  
37 participating observer. The focus groups will consist of three rounds: Round 1: preparatory  
38 phase; Round 2: (i) round-robin listing, (ii) developing a group list of patient-preferred  
39 outcomes, (iii) eliciting personal preferred outcomes, (iv) eliciting preferred outcomes in the  
40 actual stage of RA; Round 3: exploring the view of participants on the evolution of their  
41 patient preferred outcomes over the past year. The second round of the focus groups was  
42 inspired by the Nominal Group Technique methodology (NGT).<sup>42</sup> NGT is a consensus  
43 method that creates two types of data: (i) written ideas and prioritization, and (ii) the wider  
44 discussion, generating and clarifying ideas.<sup>43</sup> Our interest for using a prioritizing methodology  
45 is firstly, to create discussion between participants about a potential inconvenient topic; and  
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3 secondly, to capture participants' underlying reasoning regarding preferences in outcomes. It  
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5 is anticipated that focus groups will last about 60 minutes.  
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### 8 9 Individual interviews ( $t_2$ )

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11 If necessary, the interviewer of  $t_1$  will conduct individual interviews at  $t_2$ . The interview guide  
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13 for these interviews is slightly adapted compared to  $t_1$  in order to question participants about  
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15 their view on changes in their preferred outcomes over time.  
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### 18 19 Procedures at both time points

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21 Both individual interviews and focus groups will be held at a neutral and convenient location,  
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23 and will be audio-recorded and transcribed verbatim according to transcription guidelines.<sup>44</sup>  
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27 At both time points, the following information will be obtained. Prior to the (focus group)  
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29 interview, participants will document socio-demographic information. They will report about  
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31 their general health, level of pain and fatigue during the past week on a visual analog scale  
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33 after the interviews to avoid influencing patient opinion in advance. Clinical information will be  
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35 extracted from the medical records by the local health professionals and shared with the  
36  
37 local principal investigator. A detailed overview of all collected variables can be found in  
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39 Supplementary file 2.  
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### 42 43 **Data analysis**

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45 Data analysis will be conducted at two levels: (i) the local analyses of  $t_1$  and  $t_2$  data, followed  
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47 by the longitudinal analysis; (ii) the meta-analysis with locally interpreted local data. The  
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49 process of data analysis was based on several frameworks, which is summarized in Figure  
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### 54 55 The local analyses

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3 In every country, the analysis process will be a team activity involving patient  
4 representatives. Preferably two researchers, including at least the local lead investigator, will  
5 independently code the interview transcripts. Data analysis will start after the first interview or  
6 focus group.  
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12 The local researchers will follow the steps that are presented in Qualitative Analysis Guide of  
13 Leuven (QUAGOL) to analyze the interview data of  $t_1$  and  $t_2$ .<sup>45</sup> The central activity in  
14 QUAGOL is the constant comparison process: between researchers' interpretations and the  
15 actual participant story, as well as to check new ideas for their presence in previous  
16 interviews. QUAGOL divides data analysis into two phases.  
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21 The first phase suggests five steps of preparation, implying only paper and pencil work: 1)  
22 rereading of the transcript to get knowledge of what the interview is about, and highlighting  
23 the relevant fragments; 2) preparing a narrative summary by describing the key story lines  
24 close to participants' words; 3) schematically describing the key ideas of the interview in a  
25 conceptual scheme; 4) fitting test and adaptation of the conceptual scheme by going back to  
26 the transcript; 5) looking for common ideas/concepts across conceptual schemes as a first  
27 comparison with the other interviews.  
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32 The second phase comprises another five steps, representing the actual coding process: 6)  
33 creating a common code list, without hierarchical structure and based on the insights from  
34 the refined conceptual schemes; 7) coding of each significant passage in a qualitative  
35 software program, while critically reviewing and refining the introduced code list; 8) defining  
36 the concepts by looking across-cases and reviewing all citations connected to a concept; 9)  
37 integration of all concepts in one story line that answers the research question, followed by  
38 verification of this overarching framework against all interviews and interview schemes; 10)  
39 describing the results.  
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54 QUAGOL is not specifically developed for focus group analysis. Therefore, the group  
55 process will also be analyzed (i.e., how the conversation in the group is organized,  
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3 developing and changing), as well as the differences within and between the groups will be  
4 taken into account.<sup>25</sup>  
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9 For the longitudinal analysis, the local teams will merge their data of  $t_1$  and  $t_2$ , in which  
10 meaningful individual statements will be extracted and compared between time points. There  
11 are no universal frameworks for analyzing longitudinal qualitative data. The local teams will  
12 be guided by the method described by Saldaña,<sup>46 47</sup> who developed a 16-question template  
13 including (i) framing questions to help focusing on the context and conditions that influence  
14 changes over time; (ii) descriptive questions to describe what kinds of changes occur; and  
15 (iii) analytic and interpretive questions to reach richer levels of analysis.  
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#### 24 The meta-analysis

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26 The findings of the three independently performed qualitative studies will be combined in a  
27 meta-analysis. Several methods for synthesizing qualitative studies have been developed,<sup>48</sup>  
28 with some studies also using a combination of methods.<sup>49</sup> The methodology developed for  
29 EQPERA is inspired by the principles of meta-ethnography as practiced by Britten et al.,<sup>50</sup>  
30 and by the coding process of QUAGOL (preparatory phase) that is based on grounded  
31 theory principles.<sup>45</sup> We combined key methodological elements of both approaches and  
32 summarized these into four steps: 1) describing each case; 2) recognizing differences,  
33 similarities and patterns across cases; 3) disentangling differences and similarities across  
34 cases; 4) fitting-test of the meta-interpretations.  
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46 The findings of the participating countries will be integrated by face to face interaction  
47 between the different local teams about their data in a consensus meeting. Local findings will  
48 be translated into English. The local teams of Belgium, The Netherlands and Sweden will at  
49 least consist of the principal investigator, a patient research partner and a rheumatologist to  
50 achieve an interdisciplinary view and prevent bias due to solo interpretations. A senior  
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3 researcher of the EQPERA team (YH), who is not linked to the local teams and data, will  
4 moderate the meeting. Below, we describe our stepwise approach.  
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### 8 *Step 1: Describing each case*

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10 In step 1, the aim is to understand the course and results of each study on its own. Each  
11 country will be viewed as a case, with each case reflecting the overarching story of all local  
12 participants.  
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16 The lead investigators (KE, IL, EM) will present their findings (including quotes) and  
17 conclusions, covering: (i) the name and description of the patient-preferred outcomes; (ii)  
18 when, where, why, and in which circumstances they were put forward by the participants; (iii)  
19 the change through time of the description participants attached to the different outcomes.  
20  
21 Furthermore, they will report about study details, using three short reports:<sup>45</sup> 1) a descriptive  
22 report, including what is specific to the participants, the treatment strategy, the research  
23 group and the healthcare system; 2) a methodological report, including deviations from the  
24 protocol, such as modifications to the interview guide, recruitment problems and level of data  
25 saturation; 3) a content report, including the main message derived from the data. A standard  
26 form will be used to enhance uniformity across presentations. The three cases will be  
27 presented one by one without immediate cross-comparison. After the case description, local  
28 teams will have familiarized with the other team's data and the particular context in each  
29 country.  
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42 In preparation of step 2, each team will individually reflect upon the following questions to  
43 stimulate the across-case analysis: 'What do I hear in every case?', 'What do I only hear in  
44 our case?', 'What do I not hear in our case?'. Furthermore, they will write down the patient-  
45 preferred outcomes they identified (codes and concepts) on color-coded sticky notes, each  
46 country representing another color, to support visually the comparison of the local findings in  
47 step 2.  
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### 56 *Step 2: Recognizing differences, similarities and patterns across cases*

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3 In step 2, the aim is to translate concepts from one study to another,<sup>50</sup> to determine how  
4 studies are related (i.e., what emerges across cases) and to recognize what is typical for  
5 each case.  
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8 An affinity diagram will be created to organize the multinational data.<sup>51</sup> The patient-preferred  
9 outcomes of the three studies will be displayed side by side (using the color-coded sticky  
10 notes). Their meaning will constantly be compared from one country to another in order to  
11 identify common and recurring, as well as conceptually different outcomes. We will start with  
12 a small set of concepts including the higher level concepts of each study, after which we will  
13 refine our first interpretations by discussing the lower-level codes.<sup>45</sup> During this process  
14 similar outcomes will be grouped if possible (by replacing the sticky notes), and we will look  
15 specifically for subtle differences between grouped outcomes.  
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18 After reaching consensus on similarities and differences, a 'saturation grid' will be completed  
19 in preparation of step 3. This is a technique used in qualitative studies to identify covered  
20 (sub)themes in each interview and decide on data saturation.<sup>52</sup> However, we will use a  
21 prespecified grid to identify the coverage of outcomes across the three studies.<sup>50</sup> Firstly, the  
22 grouped outcomes will be renamed. Secondly, all outcomes will be listed, meaning that each  
23 outcome of each local study is encompassed by one of the renamed outcomes in the grid.  
24 The main explanation of each outcome will be added. Thirdly, each country will represent a  
25 column and their sticky notes will be pasted next to the outcome in the grid that fits best the  
26 description on the sticky note. Hence, the empty cells will represent the outcomes that do not  
27 emerge across countries. By completing the grid, an overview will be developed of  
28 differences and similarities across cases.  
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### 48 *Step 3: Disentangling differences and similarities across cases*

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50 In step 3, the aim is to explain the recognized differences and similarities by discussing why  
51 (or why not) certain outcomes emerge in a particular country or across countries.  
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54 Starting from the saturation grid (step 2), we will first go back to the methodological  
55 considerations and contextual features (step 1), before looking for possible cultural  
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3 explanations. The group discussion will be an essential element in this step. For this reason  
4 we will view this discussion as a focus group, producing data that will be audio recorded and  
5 transcribed verbatim. After step 3, we will have obtained consensus on cross-cultural  
6 variation in patient-preferred outcomes in early RA.  
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10 In preparation of step 4, the local teams will separately draft a written summary of the  
11 discussion immediately after the focus group and with special attention to how their case was  
12 similar or different to the other cases.  
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#### 16 17 18 *Step 4: Fitting-test of the meta-interpretations*

19 In step 4, the aim is to verify the appropriateness of the interpretations made during the focus  
20 group (step 3) regarding similarities and differences across countries.  
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26 Each local team will perform a fitting-test of common and own meta-interpretations with their  
27 local data. The local researchers will go back to their data, after rereading the focus group  
28 transcript and with their written summary in mind. Two questions will need to be answered:  
29 (1) Do the contextual interpretations actually reflect what is seen in our data? Is certain  
30 context information overlooked in the focus group? (2) Can we support the meta-  
31 interpretations with quotes that typically describe the perspective of our participants? During  
32 conference call meetings, the meta-interpretations will be adapted, completed or refined  
33 based on the fitting-test in each country.<sup>45</sup>  
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#### 44 **Patient and Public Involvement**

45 Patients were involved in every step of the research project, as described throughout the  
46 paper. Research findings will be disseminated at Patient and Public Engagement events  
47 where appropriate.  
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#### 52 **Enhancing data quality and methodological rigor**



## Quality assurance

EQPERA is a large, multicountry, multicenter, multilingual, longitudinal qualitative research project. To yield sound results, several strategies are applied to ensure trustworthiness. These are: (i) recruitment of a qualified and motivated team; (ii) use of forward-backward translation procedures; (iii) uniformity in recruitment, conducting the interviews and focus groups, transcription of audio files, data coding, data storing, and reporting; (iv) interdisciplinary team analysis (v) training of local staff to the protocol and hands-on guidance by the project leader. In Table 1, a detailed description is provided of the used strategies according to four quality criteria (i.e., credibility, dependability, confirmability, and transferability).<sup>53 54</sup>

## Quality appraisal

As the findings of independently performed primary studies will be combined, quality is an important aspect to consider requiring a formal system for appraisal. The local teams will use a quality reporting tool to support a consistent use of methods and documentation across studies. Johnson et al. provided a useful template,<sup>51</sup> based on the consolidated criteria for reporting qualitative research,<sup>55</sup> and the quality criteria suggested by Mays and colleagues.<sup>56</sup> In EQPERA, several items were added regarding data management and quality appraisal in qualitative research.<sup>32 44 57-59</sup> Our tool comprises 50 items regarding four domains: 1) research team and reflexivity; 2) study design; 3) analysis and findings; 4) data management strategies (Supplementary file 3).

**Table 1** Applied quality assurance strategies in EQPERA, described for each research stage, according to Lincoln and Guba's framework for evaluating trustworthiness.<sup>53</sup>

Research stage	Employed strategies for supporting trustworthiness	Assessing quality:			
		(1) Credibility (internal validity)	(2) Dependability (reliability)	(3) Confirmability (objectivity)	(4) Transferability (generalizability)
<b>Study design</b>	- developed around the patient perspective and in collaboration with patient representatives	•			
	- triangulation of interview methods	•			
	- addressing potential drop-out at $t_2$	•			
<b>Establishment of the EQPERA team</b>	- recruitment of a qualified team, with a passion for the topic:	•	•	•	•
	○ skilled in conducting qualitative research				
	○ familiar with the patient population				
<b>Protocol development and implementation</b>	○ including patient research partners				
	- a clear understanding of the overall project objective by all co-workers		•		•
	- use of detailed study protocol, including a methods and analysis plan, an interview protocol, a data management plan, and templates	•	•		
	- training of local staff to the protocol (project leader) prior to patient recruitment of $t_1$ and data collection of $t_2$	•	•		
	- monitoring of local progress and hands-on guidance (project leader)		•		•
<b>Sampling and recruitment</b>	- documentation of local decisions (use of a research journal):	•	•	•	•
	○ when, why, what changes, and who was involved in making this decision (e.g., modifications to the interview guide)				
	○ personal and/or practical comments				
<b>Sampling and recruitment</b>	- purposive sampling informed by simultaneous data collection and analysis	•			•
	- multicountry and multicenter recruitment	•			•

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	- applying a definition for data saturation	•			•
	- use of an enrollment template to support heterogeneity in the local samples and systematically keep records			•	
<b>Data collection</b>	- semi-structured interview guides:	•	•	•	
	o the same main interview questions in every country				
	o collaboration with patient research partners to support clarity and understandability of interview questions				
	o forward-backward translation				
	o the same key points in the introduction				
	- use of a data collection template and at least 2 audio recorders/interview to prevent missing data			•	
	- verbatim transcription of the audio-recorded data			•	
	- use of transcription guidelines			•	
	- neutral and convenient interview location	•			
$t_1$	- maximum 2 interviewers/country			•	
	- maximum 2 interviews/day per interviewer to avoid interview burden and take time to reflect upon each interview				
$t_2$	- the interviewer of $t_1$ is moderator of the focus groups			•	
	- 1 moderator/country and the same observer(s) for each focus group				
<b>Data analysis</b>	- independent coding by at least 2 researchers	•			•
<b>Local level</b>	- data collection and analysis in parallel	•			
	- constant comparison method	•			
	- use of field notes	•			•
	- reflection after each interview/focus group: descriptive, content and methodological report	•			•
	- use of a qualitative software program			•	
	- peer debriefings: more frequently early in de coding process	•			•
	- looking at data from multiple perspectives, including collaboration with patient researchers to help understand and describe the data	•			•
	- uniform procedure across countries based on established frameworks			•	•
<b>International level</b>	- translation of the local findings and conclusions using a structured forward-backward procedure, supported by professional translators			•	
<b>Reporting</b>	- use of guidelines for reporting the synthesis of qualitative research <sup>80</sup>				•

$t_1$ : time point 1= three to six months after start of the initial treatment for early rheumatoid arthritis;  $t_2$ : time point 2= at least one year after start of the initial treatment for early rheumatoid arthritis.

## ETHICS AND DISSEMINATION

### Ethical considerations

EQPERA will apply the principles established in the Declaration of Helsinki.<sup>61</sup> Participants will provide written informed consent before data collection of  $t_1$  and  $t_2$ . Only coded and interpreted data will be shared between the local teams for the meta-analysis. Ethics approval for the original studies were granted by the responsible institutional review boards.

### Dissemination of results

Every country will prepare a publication on their national findings. Two EQPERA main papers are foreseen: 1) the present paper describes the rationale, design and methods of EQPERA; 2) a publication on the results of the meta-analysis. Next to peer-reviewed publications, we will also disseminate our findings in (inter)national research presentations, and also patient organizations will be updated about the study findings.

## CONCLUSION

In EQPERA, the aim is to confirm the Belgian findings on patient-preferred outcomes in early RA in a European context, and provide a study protocol that has the potential to offer a methodological framework for further exploration of transferability in other contexts. Ultimately, study findings will be used to inform and optimize current care initiatives in early RA in order to address the unmet need of patient-centered care in RA.

## ACKNOWLEDGEMENTS

We wish to thank Patrick Verschueren and Bernadette Dierckx de Casterlé for sharing their methodological advises on the meta-analysis approach.

### **Author contributions**

The following authors were involved in this study: Kristien Van der Elst (KE), Ann Bremander (AB), An De Groef (AG), Ingrid Larsson (IL), Elke Mathijssen (EM), Johanna Vriezekolk (JV), René Westhovens (RW), Yvonne van Eijk-Hustings (YH). KE and RW had the main idea of the study. KE, AB, AG, IL, EM, JV, RW and YH contributed to the design of the study. KE, YH and RW drafted the manuscript. KE, AB, AG, IL, EM, JV, RW and YH were involved in the editing of the manuscript. All authors read and approved the final version of the manuscript. Apart from the first and last author, the other authors are listed in alphabetical order.

### **Funding statement**

This work was supported by an unrestricted educational grant of Bristol-Myers Squibb, by a travel grant from Fonds voor Wetenschappelijk Reuma Onderzoek (fund for Scientific Rheumatism Research) (Belgium) and by Southern Health Care Region (Sweden).

### **Competing interest statement**

None declared.

### **Patient consent**

Will be obtained.

### **Ethics approval**

The Netherlands: the Medical Research Ethical Committee of Arnhem-Nijmegen waived ethical approval since the medical research involving human subjects act did not apply to this study; Sweden: ethical approval was obtained from the Regional Ethical Review Board at Lund University, Sweden; Belgium: ethical approval was obtained from the Human Research Ethics Committee of the University Hospitals Leuven.

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5 **Data sharing statement**  
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7 Not applicable.  
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For peer review only

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29 **Figure 1** Overview of the European, longitudinal, multimethod qualitative research  
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35 **Figure 2** Forward-backward translation framework applied to translate the interview  
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37 questions and procedures  
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41 **Figure 3** Simplified outline of the used frameworks,<sup>25 45-47 50</sup> and the included steps in  
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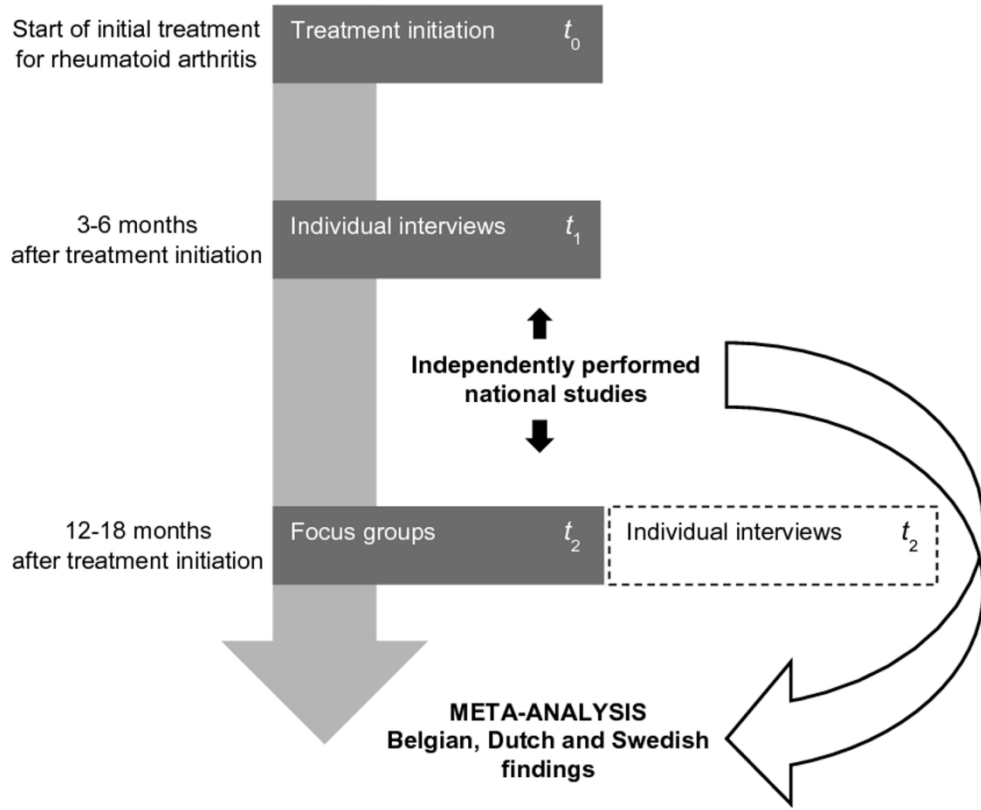


Figure 1 Overview of the European, longitudinal, multimethod qualitative research design. *t*: time point.

166x138mm (300 x 300 DPI)

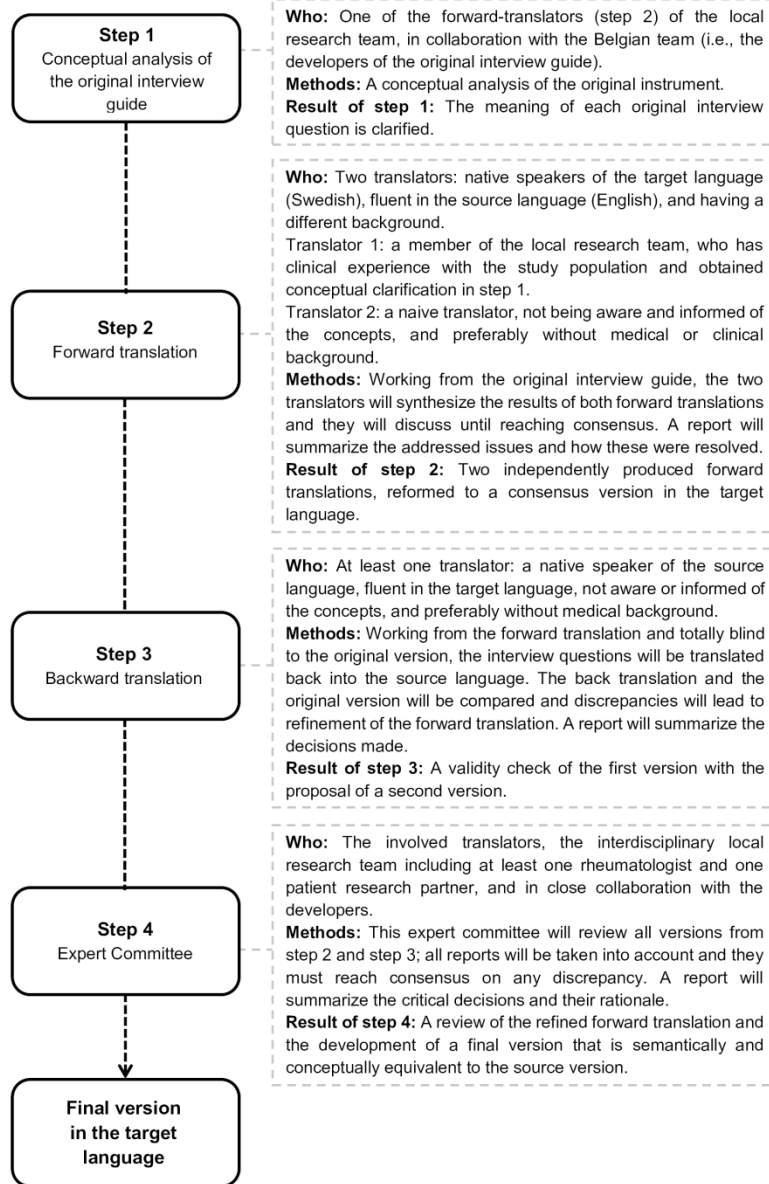
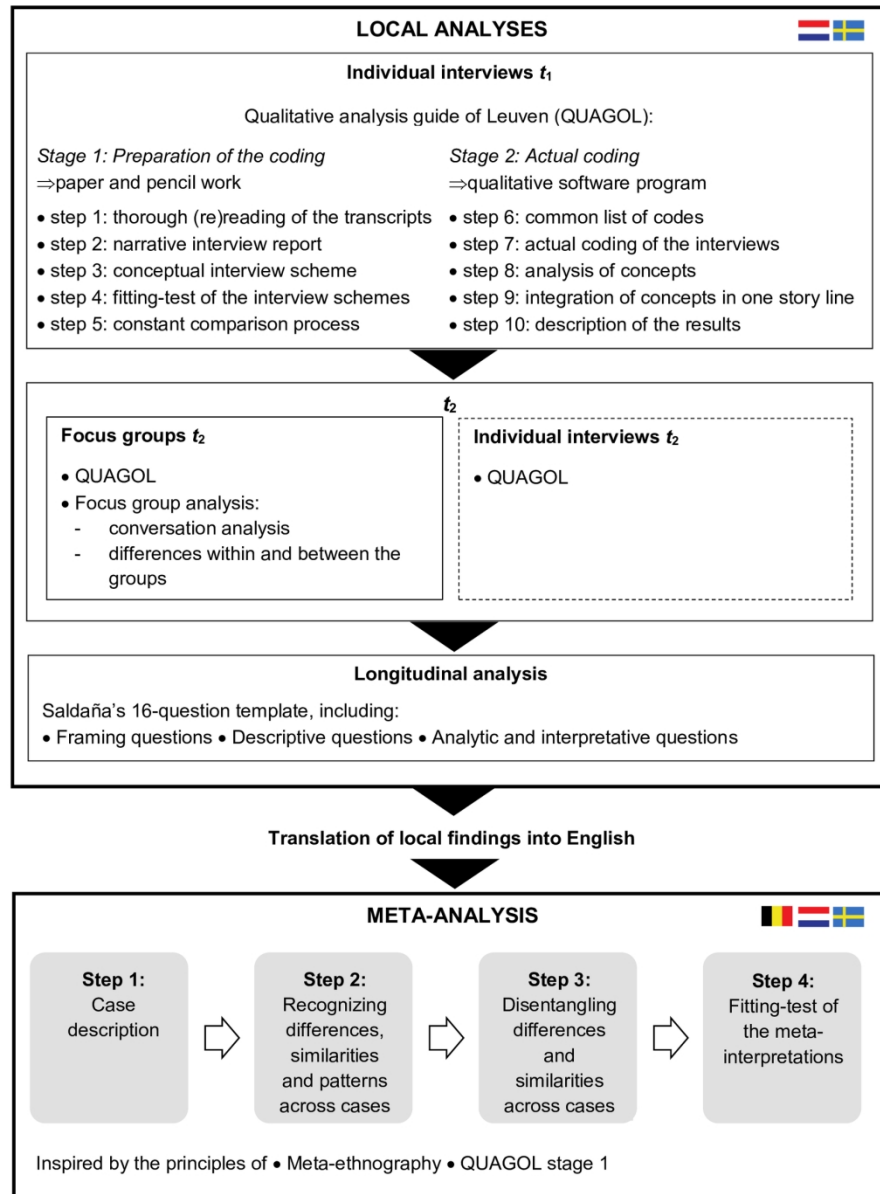


Figure 2 Forward-backward translation framework applied to translate the interview questions and procedures.

163x249mm (300 x 300 DPI)



45 Figure 3: Simplified outline of the used frameworks,<sup>25 45-48</sup> and the included steps in the local analyses and  
46 the meta-analysis.

47 146x197mm (300 x 300 DPI)

**Supplementary file 1** Main interview questions and procedures for the individual interviews ( $t_1$  and  $t_2$ ) and focus groups ( $t_2$ ). Most aspects of the methods of  $t_1$  and  $t_2$  are adopted from the original Belgian study\*

### Context questions

- What type of treatment are you currently receiving?
- Have there been any changes in your treatment plan? If so, why and what type of changes?

### Individual interviews at $t_1$

#### *Preparatory phase (5 to 10 minutes)*

To set the scene for the interview, participants were asked to write down as many keywords describing:

- the impact of rheumatoid arthritis (RA) on their life
- which outcomes of their illness and treatment they considered most important.

#### *Start of the interview*

The interviews began by discussing participants' written answers to those 2 questions. Participants were asked to elaborate on their keywords:

- Can you tell me how RA affects your daily life?
- Which outcomes of your illness and antirheumatic treatment are important to you at this moment?

#### *Proceeding of the interview*

The order of the other interview questions was determined by the participants' answers during the interview.

- How has the treatment been working for you so far?
- How do you decide whether or not your treatment is working?
- What made you decide to start treatment?
- What were your expectations of your antirheumatic treatment at the start of treatment?
- To what extent do the expectations you had at the start of your treatment match your current expectations?

Three questions were added after the first interviews: Other patients talked about 1) taking less medication, 2) returning to a normal life, 3) feeling better. Is this something you recognize? What do you feel about that?

Probing questions: Could you tell me more about that? Could you give an example?

#### *End of the individual interview*

Is there anything else you would like to add?

### Focus groups at $t_2$

#### *Round 1: preparatory phase (5 to 10 minutes)*

The moderator introduced the phenomenon of interest, after which each group member was asked to independently prepare answers to the question below by writing down as many keywords as possible. Each answer was written on a separate sticky note.

- Which outcomes of your illness and antirheumatic treatment are important to you at this moment?

Next, participants were asked to try to order their sticky notes on a vertical scale, from most important (top) to least important (bottom).

Participants were simultaneously asked to think about the following questions:

- What important treatment results have already been achieved?
- At present, is there anything you would like to change or improve regarding your disease or treatment?



1  
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3  
*Round 2, step 1: round-robin listing*

4 All group members were asked to reveal and clarify, one by one, their personally preferred  
5 outcomes in order of importance. Meanwhile, the observer wrote these outcomes on a flipchart  
6 in front of the group.

- 7 - Who would like to share your personally valued outcomes with the group, in order of  
8 importance?  
9 - Could you please clarify why these outcomes of your disease and antirheumatic treatment  
10 are important to you?  
11 - Why did you designate that specific outcome to be the most important?  
12 - Is there anything else you would like to add?

13  
14 *Round 2, step 2: developing a group list of patient-preferred outcomes*

15 The group was asked to generate a consensus list by reviewing and merging all recorded outcomes  
16 and agreeing on the name and properties of each outcome on the list.

- 17 - Could any of the individual expectations be grouped?  
18 - Who would like to suggest a name and meaning for this outcome?  
19 - Do you think all the important outcomes are mentioned on the group list?  
20 - Is there anything else you would like to add?

21 *Round 2, step 3: eliciting personal preferred outcomes*

22 Starting from the consensus list of patient-preferred outcomes that resulted in step 2, each group  
23 member was asked to independently try to select his or her 5 top outcomes from this list, using  
24 the sticky note ordering scheme.

25 *Round 2, step 4: eliciting preferred outcomes in the actual stage of RA*

26 The group was then asked to discuss a collective top 5 outcomes and to consider influencing  
27 factors.

- 28 - Looking at the group list, what outcome would you order as most important?  
29 - What outcome would you order second...fifth?  
30 - Can you tell us why this outcome is either important to you or not?  
31

32 *End of round 2*

33 That is it for the second round. Is there anything else to add?

34 *Round 3: exploring the view of participants on the evolution of their patient-preferred outcomes over*  
35 *the past year*

36 The focus groups ended by exploring the participants' views on potential changes in personally  
37 preferred outcomes over time. During the individual interview of last year, you were asked for  
38 your preferred illness and treatment outcomes. In the meantime, you have gained more  
39 experience with your disease and treatment and the critical disease stage has passed.

- 40 - Do you feel that other results are now more important to you than the ones you identified at  
41 the start or during your interview last year?  
42 - Could you explain why this has or has not changed?  
43 - Are there outcomes that are now more, less, or no longer important to you?  
44 - Why do you think that these are now more or less important than a year ago, or are no longer  
45 important? What may have caused this change in importance?  
46 - Do you have an example of an outcome that has changed in importance compared to that  
47 outcome in the early disease stage? Why do you think this has changed? Could you clarify  
48 this in more detail?  
49 - In general you mention (more or less) similar/different outcomes of importance compared to  
50 last year (in the early disease stage). What is your opinion on this observation?  
51

52 *End of round 3*

53 This is the end of the third round. Is there anything else to add?  
54  
55  
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3 Probing questions: Is this outcome also important or not important to other group members? Are there  
4 any suggestions from other group members? Is there anyone who has a different opinion on the  
5 matter? Is it difficult for you to share your opinion on this? Does everyone agree? Who agrees or  
6 disagrees and why? Who would like to add something?

7 *End of the focus group*

- 8 - What is your general conclusion about today's focus group on preferred and important  
9 outcomes of disease and treatment in the actual disease stage?  
10 - To summarize, you talked about [...]. Do you agree with this summary of today's focus group?

### 11 **Individual interviews at $t_2$**

12 *Preparatory phase (5 to 10 minutes)*

13 Please, consider the next 5 to 10 minutes the question below by writing down as many keywords  
14 as possible. The interviews will begin by discussing your written answers to this question:

- 15 - Which outcomes of your illness and antirheumatic treatment are important to you at this  
16 moment?

17 *Start of the interview*

- 18 - Can you tell me what you have written down? So, which outcomes of your illness and  
19 antirheumatic treatment are important to you at this moment?

20 *Proceeding of the interview*

21 Exploring patient-preferred outcomes

- 22 - How has the treatment been working for you so far?  
23 - To what extent do the expectations you had at the start of your treatment match your current  
24 expectations?

25 Exploring the view of participants on the evolution of their preferred outcomes over the past year

26 Last year, during the interview, you mentioned that the following outcomes of your treatment were  
27 important: ..... ( $t_1$  keywords of the  $t_2$  participant).

- 28 - Do you feel that other results are now more important to you than the ones you identified at  
29 the start or during your interview last year? Could you explain why this has or has not  
30 changed?  
31 - Are there outcomes that are now more, less, or no longer important to you?  
32 - Why do you think that these are now more or less important than a year ago, or are no  
33 longer important? What may have caused this change in importance?  
34 - Do you have an example of an outcome that has changed in importance compared to that  
35 outcome in the early disease stage? Why do you think this has changed? Could you clarify  
36 this in more detail?

37 Patient-preferred outcomes compared to the focus groups at  $t_2$

38 During the focus groups the following 5 treatment outcomes were found to be most important: 1)  
39 preferred outcome; 2) preferred outcome; 3) preferred outcome; 4) preferred outcome; 5)  
40 preferred outcome.

- 41 - I wonder if you recognize yourself in this? Could you explain why this is or is not the case?

42 *End of the individual interview*

43 Is there anything else you would like to add?

44  $t_1$ : time point 1= 3-6 months after start of the initial treatment for early rheumatoid arthritis;

45  $t_2$ : time point 2= 12-18 months after start of the initial treatment for early rheumatoid arthritis.

46 \*Van der Elst K, Meyfroidt S, De Cock D, et al. Unraveling Patient-Preferred Health and Treatment  
47 Outcomes in Early Rheumatoid Arthritis: A Longitudinal Qualitative Study. Arthritis Care Res (Hoboken)  
48 2016;68(9):1278-87.

**Supplementary file 2** EQPERA Data collection template

<b>Enrollment and interview logistics (<math>t_1</math> and <math>t_2</math>)</b>	
Respondent ID	ID number
Date of birth	dd/mm/yyyy
Gender	man, woman, X
Respondents' place of residence	postal code, location
Responsible recruiter	function, name, contact details
Rheumatology center	name, location
Type of rheumatology center	academic hospital, general hospital, private practice
Treating rheumatologist	name
Date of diagnosis	dd/mm/yyyy
Symptom duration	in months, [date of diagnosis - date of symptom onset]
Disease duration	in months; calculated with date of diagnosis
Comorbidity	no severe comorbidities present [yes/no]
Date of RA treatment initiation	dd/mm/yyyy
Months of treatment experience at $t_1$	date interview $t_1$ - date treatment initiation = between 3-6 months
Initial treatment	the local treatment protocol for early RA: free text, no details on dosages
Initial treatment allocated according to clinical prognostic factors	yes/no
Step-down strategy	yes/no (as initial treatment strategy)
MTX-only step-up	yes/no (as initial treatment strategy)
MTX + early bridging glucocorticoids	yes/no (as initial treatment strategy)
o glucocorticoids starting dose <30mg/day	yes/no
o glucocorticoids starting dose $\geq$ 30mg/day	yes/no
Early combination therapy classical DMARDs with glucocorticoids	yes/no (as initial treatment strategy)
o number of DMARDs included	number
o glucocorticoids starting dose <30mg/day	yes/no
o glucocorticoids starting dose $\geq$ 30mg/day	yes/no
Early combination therapy classical DMARDs without glucocorticoids	yes/no (as initial treatment strategy)
o number of DMARDs included	number
Biologicals as a first hit	yes/no (as initial treatment strategy)
Responder to initial treatment (at moment of $t_1$ recruitment)	yes/no
Patient obliged or deciding to discontinue RA treatment (at moment of $t_1$ recruitment; e.g., because of safety reasons, patient's decision)	yes/no
Reason to not recruit patient	free text or N/A (not applicable)
Date of study invitation	dd/mm/yyyy (sharing of invitation letter)
Reason in case not interested in study (if shared)	free text
Invitation for $t_1$ by phone (if interested)	dd/mm/yyyy (first contact between patient and researchers)

1		
2		
3	Verbal consent for $t_1$ after phone call	yes/no
4	Contact details patient	address/phone number/email
5	Patient-preferred contact method	by phone or email
6	Date and timing of individual interview $t_1$	dd/mm/yyyy; hour
7	Location of individual interview $t_1$	home or rheumatology practice/clinic
8	Reminder for $t_1$ sent	dd/mm/yyyy
9	Reason in case interview $t_1$ was cancelled (if shared)	free text
10		
11	Respondent gave written informed consent $t_1$	yes/no
12	Interviewer $t_1$	name
13	Interviewer is involved as participant's health professional in daily practice	yes/no
14	$t_1$ respondent gave consent at $t_1$ to be contacted again for second part of study ( $t_2$ )	yes/no
15	Reason in case not interested in $t_2$ (at $t_1$ ) participation (if shared)	'Not interested to share own experiences in group', 'Feeling uncomfortable to talk in group', 'Fear for seeing other patients', 'Not interested in the story of other patients', 'Other'
16		
17	Months of treatment experience at $t_2$	date focus group - date treatment start= at least 1 year (between 12-18 months) after treatment initiation
18		
19	Invitation letter $t_2$ sent by post	dd/mm/yyyy (by researchers)
20	Invitation for $t_2$ by phone	dd/mm/yyyy (by researchers)
21	Verbal consent for $t_2$ after phone call	yes/no
22	If not interested in group interview, interested in individual interview instead?	yes/no
23	Reason in case not interested in $t_2$ (if shared)	'Not interested to share own experiences in group', 'Feeling uncomfortable to talk in group', 'Fear for seeing other patients', 'Not interested in the story of other patients', 'Other'
24		
25	Date and timing of focus group $t_2$	dd/mm/yyyy; hour
26	Location of focus group $t_2$	clinical or non-clinical setting
27	If applicable: Date and timing of individual interview $t_2$	dd/mm/yyyy; hour
28	If applicable: Location of individual interview $t_2$	home or rheumatology practice/clinic
29	Reminder for $t_2$ sent (focus group or individual interview)	dd/mm/yyyy
30	Reason in case focus group (or individual interview) $t_2$ was cancelled (if shared)	free text
31	Respondent gave written informed consent $t_2$	yes/no
32	Moderator $t_2$	name
33	Observer(s) $t_2$	name(s)
34	If applicable: Interviewer $t_2$	name
35	Are the (interviewers/) moderators/observers involved as health professionals in the participants' daily clinical care	yes/no
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55		
56	<b>Socio-demographic data: patient-reported <math>t_1</math></b>	
57	Date of birth	dd/mm/yyyy
58	Gender	man, woman, X
59	Educational level $t_1$	low, moderate, high
60		

1		
2		
3	Currently employed $t_1$	yes/no
4	Employment status $t_1$	employed, not employed, retired,
5		housewife/houseman, student
6	Marital status $t_1$	single, together unmarried, married, widower,
7		other
8	Living status $t_1$	alone, with partner and/or kids, with other
9		persons

#### Socio-demographic data: patient-reported $t_2$

11		
12	Educational level $t_2$	low, moderate, high
13		
14	Currently employed $t_2$	yes/no
15	Employment status $t_2$	employed, not employed, retired,
16		housewife/houseman, student
17	Marital status $t_2$	single, together unmarried, married, widower,
18		other
19	Living status $t_2$	alone, with partner and/or kids, with other
20		persons

#### Clinical data: patient-reported data $t_1$

23		
24	VAS general health $t_1$	100-mm visual analogue scale from best (0/100)
25		to worst (100/100)
26	VAS pain $t_1$	100-mm visual analogue scale from best (0/100)
27		to worst (100/100)
28	VAS fatigue $t_1$	100-mm visual analogue scale from best (0/100)
29		to worst (100/100)
30	Key words in preparation of $t_1$ interview	Key words describing:
31		- the impact of RA on their life
32		- which outcomes of their illness and treatment
33		they considered most important

#### Clinical data: patient-reported data $t_2$

35		
36	VAS general health $t_2$	100-mm visual analogue scale from best (0/100)
37		to worst (100/100)
38	VAS pain $t_2$	100-mm visual analogue scale from best (0/100)
39		to worst (100/100)
40	VAS fatigue $t_2$	100-mm visual analogue scale from best (0/100)
41		to worst (100/100)
42	Key words in preparation of $t_2$ focus group	Key words describing which outcomes of their
43	(/interview)	illness and treatment they considered most
44		important

#### Clinical data: health professional-reported data $t_1$ and $t_2$ (to be extracted from database/patient file)

47		
48		
49	Date of diagnosis	dd/mm/yyyy
50	Symptom duration	in months, [date of diagnosis - date of symptom
51		onset]
52	Disease duration	in months; calculated with date of diagnosis
53	Comorbidity	no severe comorbidities present [yes/no]
54	Start of treatment	dd/mm/yyyy
55	Months of treatment experience at $t_1$	date interview $t_1$ - date treatment start = between
56		3-6 months
57	Months of treatment experience at $t_2$	date focus group $t_2$ - date treatment start = at least
58		1 year
59		
60		

1		
2		
3	Initial treatment	the local treatment protocol for early RA, free text,
4		no details on dosages
5	Initial treatment allocated according to clinical	yes/no
6	prognostic factors	
7	Step-down strategy	yes/no (as initial treatment strategy)
8	MTX-only step-up	yes/no (as initial treatment strategy)
9	MTX + early bridging glucocorticoids	yes/no (as initial treatment strategy)
10	○ glucocorticoids starting dose <30mg/day	yes/no
11	○ glucocorticoids starting dose ≥30mg/day	yes/no
12	Early combination therapy classical DMARDs	yes/no (as initial treatment strategy)
13	with glucocorticoids	
14	○ number of DMARDs included	number
15	○ glucocorticoids starting dose <30mg/day	yes/no
16	○ glucocorticoids starting dose ≥30mg/day	yes/no
17	Early combination therapy classical DMARDs	yes/no (as initial treatment strategy)
18	without glucocorticoids	
19	○ number of DMARDs included	number
20	Biologicals as a first hit	yes/no (as initial treatment strategy)
21	Treatment failure in the first year	yes/no
22	Treatment failure after 1 year	yes/no
23	Patient who discontinued treatment ( $t_1$ or $t_2$ ; e.g.,	yes/no
24	because of safety reasons, patient's decision)	

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*Note.* RA: Rheumatoid Arthritis; MTX: Methotrexate; DMARDs: Disease-Modifying Anti-Rheumatic Drugs; VAS: Visual Analog Scale;  $t_1$ : time point 1= 3-6 months after start of the initial treatment for early rheumatoid arthritis;  $t_2$ : time point 2= 12-18 months after start of the initial treatment for early rheumatoid arthritis.

**Supplementary file 3** EQPERA data quality assurance reporting tool

**Domain 1: Research team and reflexivity**

Item	Guide questions/description
<i>Researcher characteristics</i>	
1. Interviewer / moderator/observer	Who conducted the interviews/ focus groups? (who observed the focus groups?) <ul style="list-style-type: none"> <li>▶ Maximum 2 interviewers at <math>t_1</math> and <math>t_2</math> /country and maximum 1 moderator at <math>t_2</math>/country</li> <li>▶ Preferably the same observer(s) for each focus group</li> </ul>
2. Credentials / background	What were the researcher's credentials? (e.g., PhD, RN)
3. Occupation	What were the researcher's occupation at the time of the study?
4. Gender	Was the researcher male or female?
5. Experience and training	What experience or training did the researcher have?
<i>Relationship with participants</i>	
6. Relationship established	Was a relationship established prior to study commencements? (e.g., health professional)
7. Participant knowledge of the interviewer	What did the participant know about the researcher? (e.g., personal goals, reasons for doing the research)
8. Interviewer characteristics	What characteristics were reported about the interviewer/moderator/observer? (e.g., bias, assumptions, reasons and interest in the research topic)

**Domain 2: Study design (a longitudinal, qualitative, explorative study)**

<i>Participant selection</i>	
9. Sampling	How were participants selected (e.g., purposively) Mono or multicenter sampling? Type of recruitment center(s)? (i.e., academic hospital, general hospital or private practice)
10. Method of approach	Who invited the participants? How were participants approached? (e.g., face to face, telephone, mail, email)
11. Sample size	How many participants were in the study? <ul style="list-style-type: none"> <li>◆at <math>t_1</math>: number of individual interviews</li> <li>◆at <math>t_2</math>: number of participants per focus group / number of individual interviews</li> </ul>
12. Non-participation	How many eligible patients could potentially be recruited? How many people were approached and how many of them refused to participate or dropped out? Reasons? (if shared) <ul style="list-style-type: none"> <li>◆Not interested in participation (refusal)</li> <li>◆Drop out (type 1): in case <math>t_1</math> interview was scheduled and cancelled</li> <li>◆Not interested in participation at <math>t_2</math> (drop out, type 2)</li> <li>◆Not interested in participation in a focus group, but willing to participate in an individual interview instead at <math>t_2</math></li> <li>◆Drop out (type 3): in case <math>t_2</math> interview was scheduled and cancelled</li> </ul>

*Setting*

13. Setting of data collection Where was the data collected?
14. Presence of non-participants Was anyone else present besides the participant and researchers?
15. Description of sample What are the important characteristics of the sample? (e.g., demographic data)

*Data collection*

16. Interview guide Were questions, prompts, guides provided by the authors?  
Was the interview guide pilot tested?  
Is it being made available?
17. Focus group guide Were questions, prompts, guides provided by the authors?  
Was the interview guide pilot tested?  
Is it being made available?
18. Audio / visual recording Did the research use audio or visual recording to collect the data?
19. Data collection method How were the data collected? ( $t_1$ : focus group or individual interview?)  
Were repeat interviews carried out at  $t_2$ ?
20. Field notes Were field notes made during and/ or after the interview or focus group?  
► if yes, please record them in the descriptive or methodological interview report.  
Were short reports prepared after each interview?
21. Duration What was the duration of the interviews or focus groups?
22. Data saturation Was data saturation discussed?  
After how many interviews was data saturation reached? (Definition in EQPERA: "if the last 3 interviews do not provide new information, insights or additional understanding to accomplish the study aims")

**Domain 3: Analysis and findings***Data analysis*

23. Number of data coders How many data coders coded the data?  
Who coded the data?
24. Independent coding Was the analysis repeated by more than 1 researcher to ensure reliability?
25. Data analysis method How were themes and concepts identified from the data? (e.g., Were themes identified in advance (framework-based) or derived from the data (data-driven?)
26. Patient research partners Did patient research partners provide feedback on the findings, and in which part(s) of the data analysis were they involved?
27. Software What software was used to manage the data?

*Reporting*

28. Quotations presented Were participant quotations presented to illustrate the themes/findings?  
Was each quote identified? (e.g., participant number, gender, age)
29. Data and findings consistent Was there consistency between the data presented and the findings?
30. Clarity of themes Were themes clearly presented in the findings?



## Domain 4: Data management strategies

### *Data recording*

31. Recording changes and decisions  
Were changes to the interview guide, the evolution in themes, deviations from the research protocol, and major local project decisions carefully documented along with the rationale for change?
- ▶ to recall decisions
  - ▶ the use of a research log book is recommended
32. Recording interview data  
Did you record the data with at least 2 audio recorders?
- ▶ to prevent missing data

### *Data storing*

33. Routinely storing of data  
Was the data (e.g., audio files, transcripts, interview reports and field notes, patient-reported and clinical data, informed consents) or the project database routinely submitted to a central data repository or a secured cloud storage system?
- ▶ to avoid missing data and to easily manage large amounts of data like in qualitative research
  - ▶ a uniform transcript header and file name could facilitate data storing (e.g., T1.number of interview.ddmmyyyy.initials of interviewer)

### *Data check*

34. Internal audit  
Could the evidence (field notes, interview transcripts, recordings, reasons for interview guide adaptations,...) be inspected by others?
35. Preventing missing data  
Did the principal investigator routinely check for missing data?

### *Data collection*

36. Recruitment flow  
Was the recruitment flow carefully documented?
- ▶ the use a research log book (enrollment spread sheet) is suggested
37. Templates  
Did you check the data collection templates and the Excel spread sheet?
38. Local interview guide  
Translation/cultural adaptation interview guide:  
Did you use the proposed framework to translate the interview guide into the source language?  
Were cultural adaptations needed?  
▶ please, record these in your research log book, together with the timing and the reason for adjustment
39. Avoiding and handling the presence of a third person  
Focus of attention during interview scheduling:  
Was the purpose of a one to one interview mentioned to the participant?  
If someone else was present, did this affect the interview/data collection?  
▶ please, reflect on this in the descriptive interview report
40. Introducing the interview  
Did you prepare and practice the interview introduction?
- ▶ to maximize the interview return
  - ▶ key words: welcoming the participant; introducing yourself; clarifying the purpose and importance of research, the importance of participant contribution, expectations regarding the participant (e.g., no good or wrong answers), role of the interviewer/moderator/observer, (t<sub>2</sub>: "rules" regarding group discussion), ethical aspects; "Any questions?"; mobile phone on silent mode)

- 1  
2  
3 41. Interview burden It is recommended to conduct 1 individual interview/day, with a maximum of  
4 2 interviews/day  
5 ▶ to avoid interview burden and to have sufficient time to reflect on each  
6 interview  
7  
8 42. Interview reports Did you write for each interview/focus group 3 short reports? (i.e., content  
9 report, descriptive report, methodological report)  
10  
11 43. Iterative process Did you use an iterative process of data collection and analysis?  
12 ▶ to support data saturation

#### *Data analysis*

- 13  
14 44. Analysis guide Did you use Qualitative Analysis Guide of Leuven (QUAGOL) to guide your  
15 data analysis?  
16 Did you use Saldaña's guiding questions for analyzing the longitudinal  
17 data?  
18  
19 45. Peer debriefings Were regular peer debriefings held?  
20 ▶ time for reflection (in team): to discuss the interview return, the  
21 development of new themes, and to question and confirm saturation of  
22 themes  
23 ▶ early in the coding and interviewing process, more frequent meetings  
24 are suggested  
25 ▶ please make a short report of each debriefing to recall discussions  
26  
27 46. Team analysis Was looked at the data in team (from different perspectives looking at the  
28 data)  
29

#### *Transcription*

- 30  
31 47. Transcription Who transcribed the data?  
32 guidelines  
33 ▶ >1 person: did you apply a uniform transcription method? (e.g.,  
34 agreements about the level of details, to obtain confidentially, to  
35 reproduce the exact words spoken)  
36 ▶ external transcriber: was the interview transcript reviewed by the  
37 interviewer on data quality and accuracy of transcribing? How did you  
38 approach this quality check?  
39

#### *Team approach*

- 40  
41 48. Patient research What was the exact role of the patient research partners in the study  
42 partners  
43  
44 49. Interdisciplinary Who joined the interdisciplinary team, and what was their contribution?  
45 team  
46

#### *Initiation session*

- 47  
48 50. Project initiation Did the local research team (at least the principal investigator) followed the  
49 initiation session lead by the project leader at  $t_1$  and at  $t_2$ ?

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51  $t_1$ : time point 1= 3-6 months after start of the initial treatment for early rheumatoid arthritis;  $t_2$ : time point  
52 2= 12-18 months after start of the initial treatment for early rheumatoid arthritis.  
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# BMJ Open

## European Qualitative research project on Patient-preferred outcomes in Early Rheumatoid Arthritis (EQPERA): rationale, design and methods of a multinational, multicenter, multilingual, longitudinal qualitative study

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2018-023606.R2
Article Type:	Protocol
Date Submitted by the Author:	22-Nov-2018
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<b>Primary Subject Heading</b>:	Research methods
Secondary Subject Heading:	Qualitative research
Keywords:	Rheumatoid Arthritis, QUALITATIVE RESEARCH, Longitudinal study, Patient Preference

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Manuscripts

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3 **European Qualitative research project on Patient-preferred outcomes in Early**  
4 **Rheumatoid Arthritis (EQPERA): rationale, design and methods of a**  
5 **multinational, multicenter, multilingual, longitudinal qualitative study**  
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## ABSTRACT

**Introduction:** Including the patient perspective is important to achieve optimal outcomes in the treatment of rheumatoid arthritis (RA). Ample qualitative studies exist on patient outcomes in RA. A Belgian study recently unraveled what matters most to patients throughout the overwhelming and rapidly evolving early stage of RA. The present study, European Qualitative research project on Patient-preferred outcomes in Early Rheumatoid Arthritis (EQPERA) was created to contribute to a more universal understanding of patient-preferred health and treatment outcomes by integrating the perspectives of patients with early RA from three European countries.

**Methods and analysis:** In EQPERA, a qualitative, explorative, longitudinal study will be implemented in The Netherlands and Sweden, parallel to the methods applied in the previously conducted Belgian study. In each country, a purposive sample of patients with early RA will be individually interviewed 3-6 months after start of the initial RA treatment and subsequently, the same participants will be invited to take part in a focus group 12-18 months after RA treatment initiation. Data collection and analysis will be independently conducted by the local research teams in their native language. A meta-analysis of the local findings will be performed to explore and describe similarities, differences and patterns across countries.

**Ethics and dissemination:** Ethics approval was granted by the responsible local ethics committees. EQPERA follows the recommendations of the Declaration of Helsinki. Two main papers are foreseen (apart from the data reporting on the local findings) for peer-reviewed publication.

**Key words:** Rheumatoid Arthritis, Qualitative research, Longitudinal study, Patient Preference

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- The specific nature of the study, in which qualitative studies are carried out in different countries and languages using a uniform methodology, is novel, and we report in a transparent way about our approach and challenges.
- As no formal meta-analysis method was present in literature applicable to our study, we developed a method based on established techniques for the synthesis of qualitative research, which can guide other researchers interested in conducting this type of research.
- Several quality enhancing strategies are applied to yield sound results in this multinational, multilingual, longitudinal qualitative study.
- The participating countries might have rather similar cultural views and healthcare systems, which would strengthen the Belgian findings, however, the study protocol offers a methodological framework for research in different parts of the world.

## INTRODUCTION

In rheumatoid arthritis (RA), the outcome landscape dramatically changed over the past decades. RA is the most prevalent chronic, auto-immune inflammatory joint disease. It was typically described as an inevitably progressive disease with a destructive and disabling natural course. The continuous growth in effective pharmacological treatments contributed to this change, but the introduction of early therapy was one of the main drivers of transformed health outcomes of patients with RA.<sup>1</sup> Nowadays, remission or at least low disease activity have become realistic treatment targets for a notable proportion of the population.<sup>2</sup>

Nevertheless, the burden of disease and unmet needs remain considerable.<sup>3 4</sup> For example, most of the patients are at working age upon diagnosis, but work disability rates remain high.<sup>5</sup> Furthermore, patients with RA indicated the need for greater emotional support, and greater psychological support to manage the impact of disease on domains such as pain, fatigue, work and leisure.<sup>6 7</sup> Hence, it seems that patient preferences are not sufficiently understood and met by health professionals. In a recent report, patient-centered care was identified as a recurrent unmet need across rheumatic diseases, including RA.<sup>8</sup> Patient-centered care can be translated as care that is guided by the values and preferences of the patients,<sup>9</sup> with patient preferences referring to the perspective, beliefs and expectations of patients regarding their health and life.<sup>10</sup> As patient-centeredness is acknowledged as one of the key dimensions of high-quality care,<sup>11</sup> integrating the patient perspective in outcome assessment is increasingly advocated to achieve optimal outcomes in the treatment of RA.<sup>12 13</sup>

Qualitative studies shed light on the different views that patients with RA have on outcome compared to health professionals. These studies revealed the importance of fatigue and independence, among others,<sup>14-16</sup> to consider in daily practice on top of the traditional measures of disease activity, i.e., the swelling of joints and laboratory parameters of inflammation. Remarkably, limited attention has been given to the perspective of recently diagnosed patients. The early disease stage is probably the most daunting period for patients,

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3 indicating specific needs and preferences.<sup>17 18</sup> The Belgian qualitative study of Van der Elst et  
4 al. provided new insights into patient-preferred outcomes in early RA, concluding that returning  
5 to 'normality' as soon as possible was the core preferred outcome, which related to aspects of  
6 disease control and participation, physical and mental aspects.<sup>19</sup> However, understanding is  
7 lacking about the transferability of these local findings to other settings and cultures.  
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15 Despite recommendations for RA management, literature shows that there are differences in  
16 how rheumatology services are viewed and practiced across countries.<sup>20 21</sup> These differences  
17 may be attributable to characteristics of the national healthcare systems, local customs,  
18 practices and values. Such cultural differences may consequently influence how patients  
19 evaluate their disease. For example, the survey study of Van Tuyl et al. demonstrated that the  
20 country in which patients were sampled resulted in slightly different key domains on how they  
21 perceived remission of disease.<sup>22</sup> Hifinger et al. showed that country of residence had an  
22 important influence on how patients with RA experienced fatigue.<sup>23</sup> It can thus be questioned  
23 whether patients in other countries would bring out other preferred outcomes.  
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37 To examine the transferability of the Belgian findings and to contribute to a more universal  
38 understanding of patient-preferred outcomes, we initiated the EQPERA consortium. EQPERA  
39 is the acronym for European Qualitative research project on Patient-preferred outcomes in  
40 Early Rheumatoid Arthritis. It is a multicenter, multilingual, longitudinal qualitative study across  
41 Belgium, The Netherlands and Sweden. The present paper reports about the international  
42 study protocol, based on the Belgian study procedures.  
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## 51 **Objectives**

52 The overall research objective in EQPERA is to explore how local context influences patient-  
53 preferred health and treatment outcomes throughout the early disease course by integrating  
54 the perspectives of patients with early RA from three European countries.  
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60 The objective is twofold:



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3 (i) to describe patient-preferred outcomes in early RA and how they change  
4 throughout the early disease course (national objective);  
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7 (ii) to identify differences, similarities and patterns in patient-preferred outcomes  
8 across the three European countries (international objective).  
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## 13 **METHODS AND ANALYSIS**

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16 The Belgian study was conducted during 2012-2013.<sup>19</sup> Based on the lessons learned and after  
17 multiple discussion rounds with the EQPERA steering group, an improved research protocol  
18 was written with the aim to implement a protocol as similar as possible in the other countries.  
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20 Start of patient inclusion was 2016 in The Netherlands and 2017 in Sweden. We intend to  
21 publish the final results by the end of 2019.  
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### 28 **Study design**

29  
30 A qualitative, explorative, longitudinal research design will be applied within a European  
31 context. As we study a research domain still lacking evidence, the use of qualitative methods  
32 is justified because we will learn from the rich descriptions of participants being shaped in their  
33 local contexts.<sup>24 25</sup> Longitudinal designs are relevant for studying complex phenomena and are  
34 specifically applicable in the context of a recent diagnosis since patients' perceptions and  
35 expectations may change during the overwhelming and rapidly evolving early disease stage.  
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37 Previous research also suggests that the way patients experience and evaluate their disease  
38 can differ depending on disease duration.<sup>15 26 27</sup>  
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50 Patients with early RA will be invited to participate at two time points (Figure 1). At  $t_1$ ,  
51 participants will be individually interviewed 3-6 months after they have started their initial  
52 treatment for RA. At  $t_2$ , participants will be invited to take part in a focus group 12-18 months  
53 after RA treatment initiation. To address a potential dropout of participants at  $t_2$ , those who  
54 decline to participate in a focus group will be invited for a repeated individual interview instead.  
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3 However, the preferred interview method at  $t_2$  remains the focus group method to align with  
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5 the original design of the Belgian study.  
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10 The reason for selecting different interview methods at  $t_1$  and  $t_2$  is based on the input of patient  
11 research partners and aims to match with patient preference in the context of a recent  
12 diagnosis. At  $t_1$ , the individual interview method is chosen because adjusting to a recent  
13 diagnosis can be seen as a primarily individual matter. Consequently, sharing personal  
14 experiences and opinions in a group setting can be too confronting at that stage of disease. A  
15 timeframe of 3-6 months after initiation of the initial RA treatment is chosen to not interfere with  
16 the diagnostic and therapeutic procedures, however, still including patients' earliest views on  
17 preferred outcomes. Furthermore, it is assumed that a few months of experience with the  
18 disease and treatment would help patients to communicate more easily about their outcome  
19 preferences.  
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33 At  $t_2$ , focus groups are chosen above the individual interview method for two reasons. Firstly,  
34 compared to the first interview moment, participants may probably feel more comfortable in a  
35 group setting, because of a grown disease perspective and the potential interaction with other  
36 patients (e.g., in the waiting room) by then. Secondly, group interactions potentially help  
37 participants to remember significant events and bring out personal thoughts, which in turn may  
38 result in more and diverse data.<sup>25 28</sup> It is reasoned that after 12-18 months of treatment  
39 experience, participants have had sufficient time to develop their view on the disease, with  
40 perhaps an observable change in their preferences accordingly.  
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### 51 **Research context**

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53 EQPERA involves three countries in Northwest Europe: Belgium, The Netherlands and  
54 Sweden. These countries have a comparable organized healthcare system including a  
55 comprehensive social security system, however, differences exist in for example their  
56 reimbursement and referral system.  
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5 Participants will receive usual care according to local standards. Across countries, a  
6 comparable early RA management is implemented in respect of current international  
7 guidelines:<sup>29 30</sup> patients should be treated (i) early: as soon as the diagnosis is made; (ii)  
8 intensively, with methotrexate in the first treatment if possible; (iii) to target: treatment  
9 adjustments according to a predefined target of sustained remission or low disease activity. In  
10 addition, there is a common culture across the countries regarding interdisciplinary team care  
11 as key in disease management, but diversity can be expected concerning implementation  
12 aspects. For example, it has been shown that there is a wide variation in the role of nurses in  
13 the management of patients with chronic inflammatory arthritis<sup>20</sup>, and in the composition of  
14 rheumatology multidisciplinary teams.<sup>31</sup>  
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28 In each country, an early RA cohort is available, the local teams include experienced qualitative  
29 researchers with a good command of the English language, and funding possibilities are  
30 available to work out their national project. The EQPERA steering group consists of team  
31 members with different disciplinary backgrounds: nurses (KE, IL, EM, YH), physiotherapists  
32 (AB, AG), a psychologist (JV), a patient representative (AG) and a rheumatologist (RW).  
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### 41 **Level of collaboration between countries**

42 Individual projects will be conducted in each country. The studies in Sweden and The  
43 Netherlands will be led by the local principal investigator (IL and EM, respectively) and  
44 supervised by the EQPERA project leader (KE), who designed and completed the Belgian  
45 qualitative study.<sup>19</sup>  
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53 Considering qualitative studies, potential language issues can be approached in two ways:  
54 either translate the transcripts and do the analysis in one place, or have the analysis done at  
55 each location and combine the data afterwards. After consideration, the project team decided  
56 that (i) data will be collected in the local settings by the local teams in their native language;  
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3 (ii) interviews will be transcribed in the original language and the transcripts will be analyzed  
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5 by the local teams; (iii) only the results of the local analysis (i.e., interpreted data) will be  
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7 combined for EQPERA purposes, and this after ending the analysis procedures and writing up  
8  
9 the findings and conclusions in every country.  
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13 Original data will thus not be reviewed by the other teams (Figure 1). Centralizing data would  
14  
15 mean translation of local transcripts to the common language in EQPERA (English).  
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17 Translation holds the risk of losing the real meaning of words,<sup>32</sup> and would be expensive and  
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19 time consuming because of the mountains of words that will be produced in every country.  
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21 Above and beyond translation issues, we assumed that local data should ideally be analyzed  
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23 by the people who are familiar with the local culture and context in order to get the most  
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25 appropriate interpretations.  
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### 30 31 **Collaboration with patient research partners**

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33 As EQPERA aims to capture the patient perspective, the project would benefit from active  
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35 collaboration with patient representatives, or those who have the lived experience of RA.  
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37 Following the recommendations of the European League Against Rheumatism for the inclusion  
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39 of patient representatives in scientific projects,<sup>33</sup> each local team will preferably collaborate  
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41 with two patient research partners.  
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46 The local principal investigators will be responsibility for coordinating this research partnership,  
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48 being guided by the FIRST (i.e., Facilitate, Identify, Respect, Support and Train) framework of  
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50 Hewlett and colleagues.<sup>34</sup> The exact level of the patient researchers' contribution will depend  
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52 on local agreements (feasibility). In general, they will help by reflecting on the methods,  
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54 formulating clear and understandable interview questions, interpreting and explaining data,  
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56 and providing feedback on the readability of the patient information leaflet and informed  
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58 consent form.  
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## Participants

Eligible patients will have to meet the following inclusion criteria: (i) confirmed diagnosis of RA, in accordance with the American College of Rheumatology/European League Against Rheumatism 2010 criteria;<sup>35</sup> (ii) time between diagnosis and start of RA treatment of less or equal than 1 year; (iii) minimum age of 18 years; (iv) speak, read and write the local language; (v) started the initial RA treatment 3-6 months ago.

## Sampling

Every country will strive to include a broad range of perspectives in their sample. To ensure this variation, participants will be purposively sampled based on their (i) age/life phase; (ii) gender; and (iii) treatment progress/treatment experience. Moreover, every country will apply a multicenter recruitment to account for possible variation in region.

Sampling in qualitative research corresponds to the assumption that collected data is of sufficient depth, i.e., representing the various views and opinions of the population with no added value of including more participants for answering the research question.<sup>36 37</sup> As there is no standardized definition of data saturation, we decided that data collection can be stopped if three consecutive interviews do not result in new themes or additional understanding (local team decision).

At  $t_1$ , we estimate that around 20 participants in every country will be needed to reach data saturation. At  $t_2$ , the sample sizes will foremost depend on the interest and willingness of participants to participate again. We aim for 4-8 participants in each focus group, which seems an appropriate number to keep the discussions manageable and stimulate contribution of every group member.<sup>36 38</sup> If possible, patient characteristics will be taken into account to create a mix of perspectives in the groups.

## Recruitment

In each country, patients are recruited from multiple centers across different geographic locations, including academic and non-academic rheumatology centers. In Belgium, patients were sampled from nine centers across Flanders. The participating centers in The Netherlands are located in Nijmegen and Woerden, and in Sweden these are located in Lund, Malmö and Halmstad. A recruitment template will help the local teams to consider the main variables for creating heterogeneity in their samples.

## Data collection

### The interview guides

The semi-structured interview guides include pre-defined topics, with open-ended questions, and probing questions to reach a higher level of detail. All questions relate to the central interview question: 'Which outcomes of your illness and antirheumatic treatment are important to you at this moment?'. In every country, the interview guides will have the same content at start, and main questions will be fixed across countries. Data collection and analysis will be performed simultaneously, making it possible to adapt the interview guides if necessary to increase participants' understanding or to reach data saturation (local team decision). If adaptations are needed, these will be documented in the local research journal.

The content of the interview guides is inspired by previous qualitative studies on outcomes from the patient perspective.<sup>14 16 39</sup> In EQPERA, Dutch and Swedish versions of the Belgian interview guides (Flemish language) will be prepared by the local teams. Given similarities between the Flemish and Dutch language, minor adaptations will be applied after discussion and consensus with the Belgian team. Forward and backward translation will be used to prepare translations into English, which then will serve as a source to translate the interview guides into Swedish. The procedure of the translation from English into Swedish is presented

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3 in Figure 2.<sup>40 41</sup> The main interview questions and the interview procedures are elucidated in  
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5 Supplementary file 1.  
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### 9 Individual interviews ( $t_1$ ) 10

11 At  $t_1$ , individual, face-to-face interviews will be conducted by maximum 2 interviewers per  
12 country, who are not involved in participants' clinical care. As the patient research partners  
13 noted that patients are in general not used to talk about outcome preferences, they will be  
14 asked to prepare written key words regarding the central interview question. The interviewer  
15 will start by elaborating on these key words. It is anticipated that interviews will last no longer  
16 than 60 minutes.  
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### 26 Focus groups ( $t_2$ ) 27

28 Focus groups will be facilitated by one of the interviewers of  $t_1$  in assistance of at least one  
29 participating observer. The focus groups will consist of three rounds: Round 1: preparatory  
30 phase; Round 2: (i) round-robin listing, (ii) developing a group list of patient-preferred  
31 outcomes, (iii) eliciting personal preferred outcomes, (iv) eliciting preferred outcomes in the  
32 actual stage of RA; Round 3: exploring the view of participants on the evolution of their patient  
33 preferred outcomes over the past year. The second round of the focus groups was inspired by  
34 the Nominal Group Technique methodology (NGT).<sup>42</sup> NGT is a consensus method that creates  
35 two types of data: (i) written ideas and prioritization, and (ii) the wider discussion, generating  
36 and clarifying ideas.<sup>43</sup> Our interest for using a prioritizing methodology is firstly, to create  
37 discussion between participants about a potential inconvenient topic; and secondly, to capture  
38 participants' underlying reasoning regarding preferences in outcomes. It is anticipated that  
39 focus groups will last about 60 minutes.  
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### 55 Individual interviews ( $t_2$ ) 56 57 58 59 60

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3 If necessary, the interviewer of  $t_1$  will conduct individual interviews at  $t_2$ . The interview guide  
4 for these interviews is slightly adapted compared to  $t_1$  in order to question participants about  
5 their view on changes in their preferred outcomes over time.  
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## 10 11 Procedures at both time points 12

13 Both individual interviews and focus groups will be held at a neutral and convenient location,  
14 and will be audio-recorded and transcribed verbatim according to transcription guidelines.<sup>44</sup>  
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19 At both time points, the following information will be obtained. Prior to the (focus group)  
20 interview, participants will document socio-demographic information. They will report about  
21 their general health, level of pain and fatigue during the past week on a visual analog scale  
22 after the interviews to avoid influencing patient opinion in advance. Clinical information will be  
23 extracted from the medical records by the local health professionals and shared with the local  
24 principal investigator. A detailed overview of all collected variables can be found in  
25 Supplementary file 2.  
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## 37 Data analysis 38

39 Data analysis will be conducted at two levels: (i) the local analyses of  $t_1$  and  $t_2$  data, followed  
40 by the longitudinal analysis; (ii) the meta-analysis with locally interpreted local data. The  
41 process of data analysis was based on several frameworks, which is summarized in Figure 3.  
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## 48 The local analyses 49

50 In every country, the analysis process will be a team activity involving patient representatives.  
51 Preferably two researchers, including at least the local lead investigator, will independently  
52 code the interview transcripts. Data analysis will start after the first interview or focus group.  
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3 The local researchers will follow the steps that are presented in Qualitative Analysis Guide of  
4 Leuven (QUAGOL) to analyze the interview data of  $t_1$  and  $t_2$ .<sup>45</sup> The central activity in QUAGOL  
5 is the constant comparison process: between researchers' interpretations and the actual  
6 participant story, as well as to check new ideas for their presence in previous interviews.  
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11 QUAGOL divides data analysis into two phases.

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13 The first phase suggests five steps of preparation, implying only paper and pencil work: 1)  
14 rereading of the transcript to get knowledge of what the interview is about, and highlighting the  
15 relevant fragments; 2) preparing a narrative summary by describing the key story lines close  
16 to participants' words; 3) schematically describing the key ideas of the interview in a conceptual  
17 scheme; 4) fitting test and adaptation of the conceptual scheme by going back to the transcript;  
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5) looking for common ideas/concepts across conceptual schemes as a first comparison with the other interviews.

The second phase comprises another five steps, representing the actual coding process: 6)  
creating a common code list, without hierarchical structure and based on the insights from the  
refined conceptual schemes; 7) coding of each significant passage in a qualitative software  
program, while critically reviewing and refining the introduced code list; 8) defining the concepts  
by looking across-cases and reviewing all citations connected to a concept; 9) integration of  
all concepts in one story line that answers the research question, followed by verification of  
this overarching framework against all interviews and interview schemes; 10) describing the  
results.

QUAGOL is not specifically developed for focus group analysis. Therefore, the group process  
will also be analyzed (i.e., how the conversation in the group is organized, developing and  
changing), as well as the differences within and between the groups will be taken into  
account.<sup>25</sup>

For the longitudinal analysis, the local teams will merge their data of  $t_1$  and  $t_2$ , in which  
meaningful individual statements will be extracted and compared between time points. There

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3 are no universal frameworks for analyzing longitudinal qualitative data. The local teams will be  
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5 guided by the method described by Saldaña,<sup>46 47</sup> who developed a 16-question template  
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7 including (i) framing questions to help focusing on the context and conditions that influence  
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9 changes over time; (ii) descriptive questions to describe what kinds of changes occur; and (iii)  
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11 analytic and interpretive questions to reach richer levels of analysis.  
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## 14 15 16 The meta-analysis

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18 The findings of the three independently performed qualitative studies will be combined in a  
19  
20 meta-analysis. Several methods for synthesizing qualitative studies have been developed,<sup>48</sup>  
21  
22 with some studies also using a combination of methods.<sup>49</sup> The methodology developed for  
23  
24 EQPERA is inspired by the principles of meta-ethnography as practiced by Britten et al.,<sup>50</sup> and  
25  
26 by the coding process of QUAGOL (preparatory phase) that is based on grounded theory  
27  
28 principles.<sup>45</sup> We combined key methodological elements of both approaches and summarized  
29  
30 these into four steps: 1) describing each case; 2) recognizing differences, similarities and  
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32 patterns across cases; 3) disentangling differences and similarities across cases; 4) fitting-test  
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34 of the meta-interpretations.  
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40 The findings of the participating countries will be integrated by face to face interaction between  
41  
42 the different local teams about their data in a consensus meeting. Local findings will be  
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44 translated into English. The local teams of Belgium, The Netherlands and Sweden will at least  
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46 consist of the principal investigator, a patient research partner and a rheumatologist to achieve  
47  
48 an interdisciplinary view and prevent bias due to solo interpretations. A senior researcher of  
49  
50 the EQPERA team (YH), who is not linked to the local teams and data, will moderate the  
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52 meeting. Below, we describe our stepwise approach.  
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### 56 *Step 1: Describing each case*

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3 In step 1, the aim is to understand the course and results of each study on its own. Each  
4 country will be viewed as a case, with each case reflecting the overarching story of all local  
5 participants.  
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9 The lead investigators (KE, IL, EM) will present their findings (including quotes) and  
10 conclusions, covering: (i) the name and description of the patient-preferred outcomes; (ii)  
11 when, where, why, and in which circumstances they were put forward by the participants; (iii)  
12 the change through time of the description participants attached to the different outcomes.  
13 Furthermore, they will report about study details, using three short reports:<sup>45</sup> 1) a descriptive  
14 report, including what is specific to the participants, the treatment strategy, the research group  
15 and the healthcare system; 2) a methodological report, including deviations from the protocol,  
16 such as modifications to the interview guide, recruitment problems and level of data saturation;  
17 3) a content report, including the main message derived from the data. A standard form will be  
18 used to enhance uniformity across presentations. The three cases will be presented one by  
19 one without immediate cross-comparison. After the case description, local teams will have  
20 familiarized with the other team's data and the particular context in each country.  
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24 In preparation of step 2, each team will individually reflect upon the following questions to  
25 stimulate the across-case analysis: 'What do I hear in every case?', 'What do I only hear in our  
26 case?', 'What do I not hear in our case?'. Furthermore, they will write down the patient-  
27 preferred outcomes they identified (codes and concepts) on color-coded sticky notes, each  
28 country representing another color, to support visually the comparison of the local findings in  
29 step 2.  
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### *Step 2: Recognizing differences, similarities and patterns across cases*

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51 In step 2, the aim is to translate concepts from one study to another,<sup>50</sup> to determine how studies  
52 are related (i.e., what emerges across cases) and to recognize what is typical for each case.  
53 An affinity diagram will be created to organize the multinational data.<sup>51</sup> The patient-preferred  
54 outcomes of the three studies will be displayed side by side (using the color-coded sticky  
55 notes). Their meaning will constantly be compared from one country to another in order to  
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3 identify common and recurring, as well as conceptually different outcomes. We will start with  
4 a small set of concepts including the higher level concepts of each study, after which we will  
5 refine our first interpretations by discussing the lower-level codes.<sup>45</sup> During this process similar  
6 outcomes will be grouped if possible (by replacing the sticky notes), and we will look specifically  
7 for subtle differences between grouped outcomes.  
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10  
11 After reaching consensus on similarities and differences, a 'saturation grid' will be completed  
12 in preparation of step 3. This is a technique used in qualitative studies to identify covered  
13 (sub)themes in each interview and decide on data saturation.<sup>52</sup> However, we will use a  
14 prespecified grid to identify the coverage of outcomes across the three studies.<sup>50</sup> Firstly, the  
15 grouped outcomes will be renamed. Secondly, all outcomes will be listed, meaning that each  
16 outcome of each local study is encompassed by one of the renamed outcomes in the grid. The  
17 main explanation of each outcome will be added. Thirdly, each country will represent a column  
18 and their sticky notes will be pasted next to the outcome in the grid that fits best the description  
19 on the sticky note. Hence, the empty cells will represent the outcomes that do not emerge  
20 across countries. By completing the grid, an overview will be developed of differences and  
21 similarities across cases.  
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### 39 *Step 3: Disentangling differences and similarities across cases*

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41 In step 3, the aim is to explain the recognized differences and similarities by discussing why  
42 (or why not) certain outcomes emerge in a particular country or across countries.  
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45 Starting from the saturation grid (step 2), we will first go back to the methodological  
46 considerations and contextual features (step 1), before looking for possible cultural  
47 explanations. The group discussion will be an essential element in this step. For this reason  
48 we will view this discussion as a focus group, producing data that will be audio recorded and  
49 transcribed verbatim. After step 3, we will have obtained consensus on cross-cultural variation  
50 in patient-preferred outcomes in early RA.  
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3 In preparation of step 4, the local teams will separately draft a written summary of the  
4 discussion immediately after the focus group and with special attention to how their case was  
5 similar or different to the other cases.  
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#### 10 11 *Step 4: Fitting-test of the meta-interpretations*

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13 In step 4, the aim is to verify the appropriateness of the interpretations made during the focus  
14 group (step 3) regarding similarities and differences across countries.  
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19 Each local team will perform a fitting-test of common and own meta-interpretations with their  
20 local data. The local researchers will go back to their data, after rereading the focus group  
21 transcript and with their written summary in mind. Two questions will need to be answered: (1)  
22 Do the contextual interpretations actually reflect what is seen in our data? Is certain context  
23 information overlooked in the focus group? (2) Can we support the meta-interpretations with  
24 quotes that typically describe the perspective of our participants? During conference call  
25 meetings, the meta-interpretations will be adapted, completed or refined based on the fitting-  
26 test in each country.<sup>45</sup>  
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#### 39 **Patient and Public Involvement**

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41 Patients were involved in every step of the research project, as described throughout the  
42 paper. Research findings will be disseminated at Patient and Public Engagement events where  
43 appropriate.  
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#### 49 **Enhancing data quality and methodological rigor**

##### 50 51 Quality assurance

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53 EQPERA is a large, multicountry, multicenter, multilingual, longitudinal qualitative research  
54 project. To yield sound results, several strategies are applied to ensure trustworthiness. These  
55 are: (i) recruitment of a qualified and motivated team; (ii) use of forward-backward translation  
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3 procedures; (iii) uniformity in recruitment, conducting the interviews and focus groups,  
4 transcription of audio files, data coding, data storing, and reporting; (iv) interdisciplinary team  
5 analysis (v) training of local staff to the protocol and hands-on guidance by the project leader.  
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7 In Table 1, a detailed description is provided of the used strategies according to four quality  
8 criteria (i.e., credibility, dependability, confirmability, and transferability).<sup>53 54</sup>  
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## 16 Quality appraisal

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18 As the findings of independently performed primary studies will be combined, quality is an  
19 important aspect to consider requiring a formal system for appraisal. The local teams will use  
20 a quality reporting tool to support a consistent use of methods and documentation across  
21 studies. Johnson et al. provided a useful template,<sup>51</sup> based on the consolidated criteria for  
22 reporting qualitative research,<sup>55</sup> and the quality criteria suggested by Mays and colleagues.<sup>56</sup>  
23  
24 In EQPERA, several items were added regarding data management and quality appraisal in  
25 qualitative research.<sup>32 44 57-59</sup> Our tool comprises 50 items regarding four domains: 1) research  
26 team and reflexivity; 2) study design; 3) analysis and findings; 4) data management strategies  
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35 (Supplementary file 3).  
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**Table 1** Applied quality assurance strategies in EQPERA, described for each research stage, according to Lincoln and Guba's framework for evaluating trustworthiness.<sup>53</sup>

Research stage	Employed strategies for supporting trustworthiness	Assessing quality:			
		(1) How congruent are the findings with reality? (2) Would the research findings be the same if the study would be replicated in essentially the same way? (3) Do the research findings emerge from the context and the respondents and not solely from the minds of the researchers? (4) Can the research be applied in other contexts?			
		(1) <b>Credibility</b> (internal validity)	(2) <b>Dependability</b> (reliability)	(3) <b>Confirmability</b> (objectivity)	(4) <b>Transferability</b> (generalizability)
<b>Study design</b>	<ul style="list-style-type: none"> <li>- developed around the patient perspective and in collaboration with patient representatives</li> <li>- triangulation of interview methods</li> <li>- addressing potential drop-out at <math>t_2</math></li> </ul>	•	•	•	•
<b>Establishment of the EQPERA team</b>	<ul style="list-style-type: none"> <li>- recruitment of a qualified team, with a passion for the topic:               <ul style="list-style-type: none"> <li>o skilled in conducting qualitative research</li> <li>o familiar with the patient population</li> <li>o including patient research partners</li> </ul> </li> </ul>	•	•	•	•
<b>Protocol development and implementation</b>	<ul style="list-style-type: none"> <li>- a clear understanding of the overall project objective by all co-workers</li> <li>- use of detailed study protocol, including a methods and analysis plan, an interview protocol, a data management plan, and templates</li> <li>- training of local staff to the protocol (project leader) prior to patient recruitment of <math>t_1</math> and data collection of <math>t_2</math></li> <li>- monitoring of local progress and hands-on guidance (project leader)</li> <li>- documentation of local decisions (use of a research journal):               <ul style="list-style-type: none"> <li>o when, why, what changes, and who was involved in making this decision (e.g., modifications to the interview guide)</li> <li>o personal and/or practical comments</li> </ul> </li> </ul>	•	•	•	•
<b>Sampling and recruitment</b>	<ul style="list-style-type: none"> <li>- purposive sampling informed by simultaneous data collection and analysis</li> <li>- multicountry and multicenter recruitment</li> </ul>	•	•	•	•

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	- applying a definition for data saturation	•		•
	- use of an enrollment template to support heterogeneity in the local samples and systematically keep records		•	
<b>Data collection</b>	- semi-structured interview guides:	•	•	•
	o the same main interview questions in every country			
	o collaboration with patient research partners to support clarity and understandability of interview questions			
	o forward-backward translation			
	o the same key points in the introduction			
	- use of a data collection template and at least 2 audio recorders/interview to prevent missing data		•	
	- verbatim transcription of the audio-recorded data		•	
	- use of transcription guidelines		•	
	- neutral and convenient interview location	•		
$t_1$	- maximum 2 interviewers/country		•	
	- maximum 2 interviews/day per interviewer to avoid interview burden and take time to reflect upon each interview			
$t_2$	- the interviewer of $t_1$ is moderator of the focus groups		•	
	- 1 moderator/country and the same observer(s) for each focus group			
<b>Data analysis</b>	- independent coding by at least 2 researchers	•		•
<b>Local level</b>	- data collection and analysis in parallel	•		
	- constant comparison method	•		
	- use of field notes	•		•
	- reflection after each interview/focus group: descriptive, content and methodological report	•		•
	- use of a qualitative software program		•	
	- peer debriefings: more frequently early in de coding process	•		•
	- looking at data from multiple perspectives, including collaboration with patient researchers to help understand and describe the data	•		•
	- uniform procedure across countries based on established frameworks		•	•
<b>International level</b>	- translation of the local findings and conclusions using a structured forward-backward procedure, supported by professional translators		•	
<b>Reporting</b>	- use of guidelines for reporting the synthesis of qualitative research <sup>60</sup>			•



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3  $t_1$ : time point 1= three to six months after start of the initial treatment for early rheumatoid arthritis;  $t_2$ : time point 2= at least one year after start of the initial  
4 treatment for early rheumatoid arthritis.  
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## **ETHICS AND DISSEMINATION**

### **Ethical considerations**

EQPERA will apply the principles established in the Declaration of Helsinki.<sup>61</sup> Participants will provide written informed consent before data collection of  $t_1$  and  $t_2$ . Only coded and interpreted data will be shared between the local teams for the meta-analysis. Ethics approval for the original studies were granted by the responsible institutional review boards.

### **Dissemination of results**

Every country will prepare a publication on their national findings. Two EQPERA main papers are foreseen: 1) the present paper describes the rationale, design and methods of EQPERA; 2) a publication on the results of the meta-analysis. Next to peer-reviewed publications, we will also disseminate our findings in (inter)national research presentations, and also patient organizations will be updated about the study findings.

## **CONCLUSION**

In EQPERA, the aim is to confirm the Belgian findings on patient-preferred outcomes in early RA in a European context, and provide a study protocol that has the potential to offer a methodological framework for further exploration of transferability in other contexts. Ultimately, study findings will be used to inform and optimize current care initiatives in early RA in order to address the unmet need of patient-centered care in RA.

## **ACKNOWLEDGEMENTS**

We wish to thank Patrick Verschueren and Bernadette Dierckx de Casterlé for sharing their methodological advises on the meta-analysis approach.

## Author contributions

The following authors were involved in this study: Kristien Van der Elst (KE), Ann Bremander (AB), An De Groef (AG), Ingrid Larsson (IL), Elke Mathijssen (EM), Johanna Vriezekolk (JV), René Westhovens (RW), Yvonne van Eijk-Hustings (YH). KE and RW had the main idea of the study. KE, AB, AG, IL, EM, JV, RW and YH contributed to the design of the study. KE, YH and RW drafted the manuscript. KE, AB, AG, IL, EM, JV, RW and YH were involved in the editing of the manuscript. All authors read and approved the final version of the manuscript. Apart from the first and last author, the other authors are listed in alphabetical order.

## Funding statement

This work was supported by an unrestricted educational grant of Bristol-Myers Squibb, by a travel grant from Fonds voor Wetenschappelijk Reuma Onderzoek (fund for Scientific Rheumatism Research) (Belgium) and by Southern Health Care Region (Sweden).

## Competing interest statement

None declared.

## Patient consent

Will be obtained.

## Ethics approval

The Netherlands: the Medical Research Ethical Committee of Arnhem-Nijmegen waived ethical approval since the medical research involving human subjects act did not apply to this study; Sweden: ethical approval was obtained from the Regional Ethical Review Board at Lund University, Sweden; Belgium: ethical approval was obtained from the Human Research Ethics Committee of the University Hospitals Leuven.

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3 **Data sharing statement**  
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5 Not applicable.  
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22 **Figure 1** Overview of the European, longitudinal, multimethod qualitative research  
23 design. *t*: time point  
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28 **Figure 2** Forward-backward translation framework applied to translate the interview  
29 questions and procedures  
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34 **Figure 3** Simplified outline of the used frameworks,<sup>25 45-47 50</sup> and the included steps in  
35 the local analyses and the meta-analysis  
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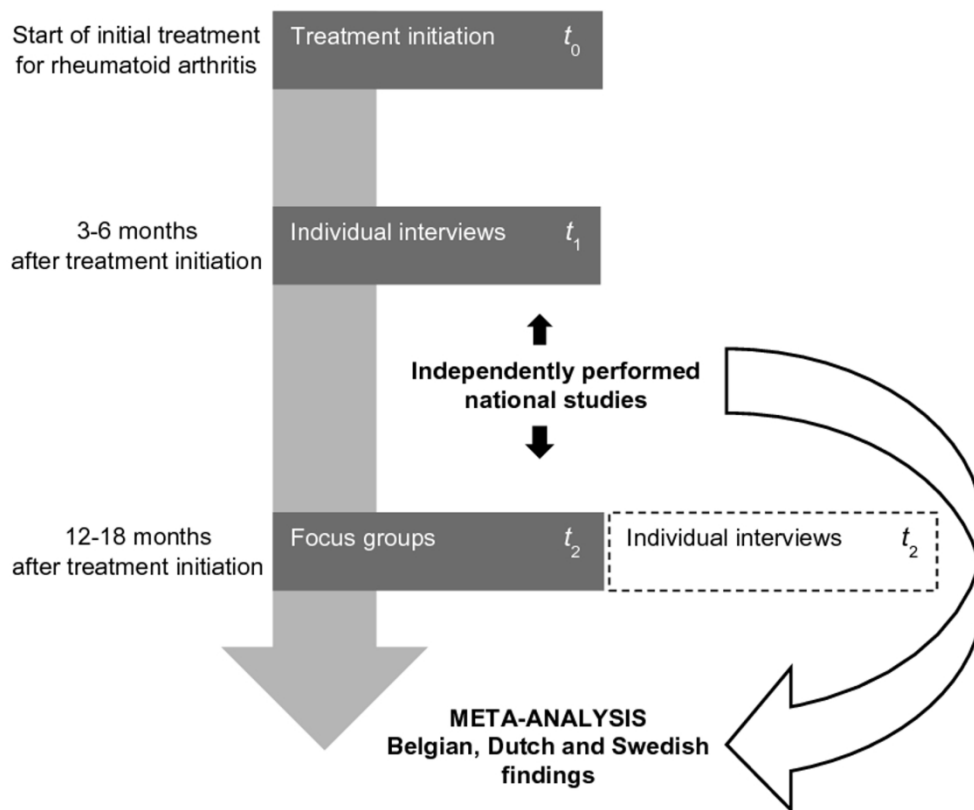


Figure 1 Overview of the European, longitudinal, multimethod qualitative research design. *t*: time point.

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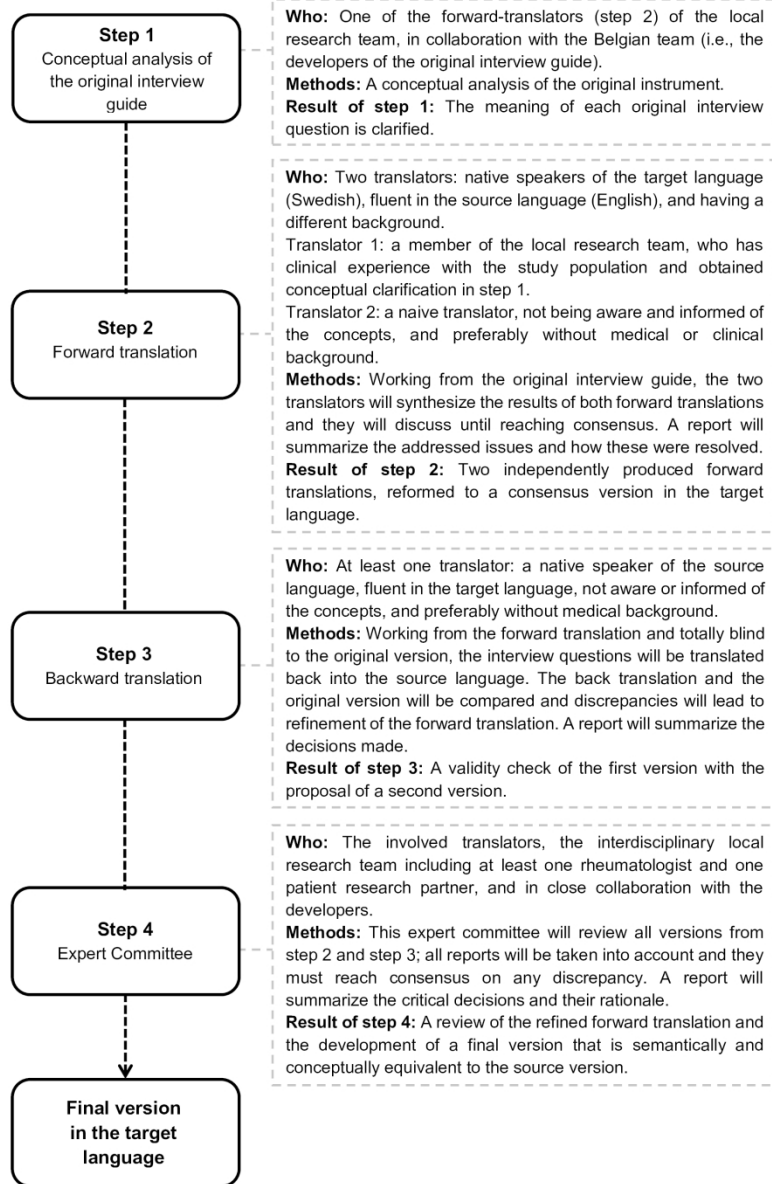


Figure 2 Forward-backward translation framework applied to translate the interview questions and procedures.

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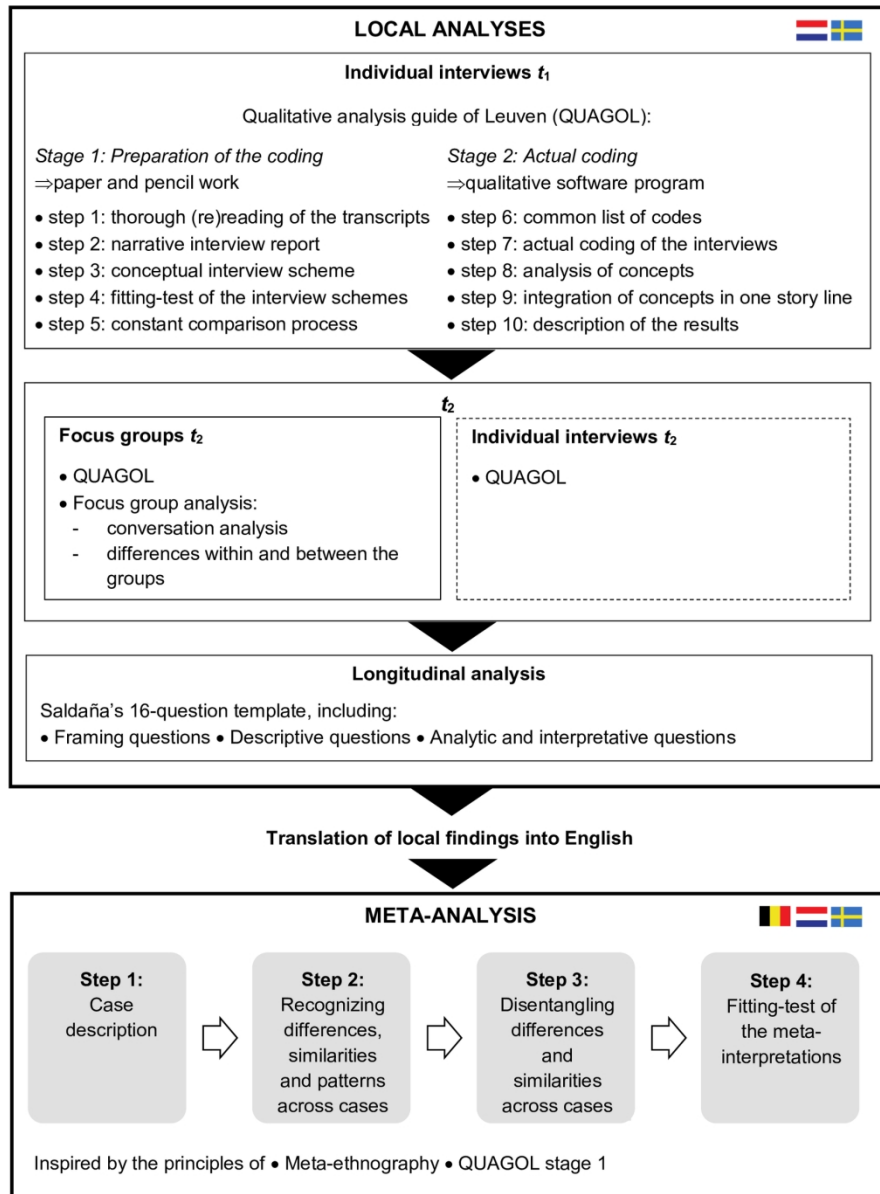


Figure 3: Simplified outline of the used frameworks,<sup>25 45-48</sup> and the included steps in the local analyses and the meta-analysis.

146x197mm (300 x 300 DPI)

**Supplementary file 1** Main interview questions and procedures for the individual interviews ( $t_1$  and  $t_2$ ) and focus groups ( $t_2$ ). Most aspects of the methods of  $t_1$  and  $t_2$  are adopted from the original Belgian study\*

### Context questions

- What type of treatment are you currently receiving?
- Have there been any changes in your treatment plan? If so, why and what type of changes?

### Individual interviews at $t_1$

#### *Preparatory phase (5 to 10 minutes)*

To set the scene for the interview, participants were asked to write down as many keywords describing:

- the impact of rheumatoid arthritis (RA) on their life
- which outcomes of their illness and treatment they considered most important.

#### *Start of the interview*

The interviews began by discussing participants' written answers to those 2 questions. Participants were asked to elaborate on their keywords:

- Can you tell me how RA affects your daily life?
- Which outcomes of your illness and antirheumatic treatment are important to you at this moment?

#### *Proceeding of the interview*

The order of the other interview questions was determined by the participants' answers during the interview.

- How has the treatment been working for you so far?
- How do you decide whether or not your treatment is working?
- What made you decide to start treatment?
- What were your expectations of your antirheumatic treatment at the start of treatment?
- To what extent do the expectations you had at the start of your treatment match your current expectations?

Three questions were added after the first interviews: Other patients talked about 1) taking less medication, 2) returning to a normal life, 3) feeling better. Is this something you recognize? What do you feel about that?

Probing questions: Could you tell me more about that? Could you give an example?

#### *End of the individual interview*

Is there anything else you would like to add?

### Focus groups at $t_2$

#### *Round 1: preparatory phase (5 to 10 minutes)*

The moderator introduced the phenomenon of interest, after which each group member was asked to independently prepare answers to the question below by writing down as many keywords as possible. Each answer was written on a separate sticky note.

- Which outcomes of your illness and antirheumatic treatment are important to you at this moment?

Next, participants were asked to try to order their sticky notes on a vertical scale, from most important (top) to least important (bottom).

Participants were simultaneously asked to think about the following questions:

- What important treatment results have already been achieved?
- At present, is there anything you would like to change or improve regarding your disease or treatment?

1  
2  
3 *Round 2, step 1: round-robin listing*

4 All group members were asked to reveal and clarify, one by one, their personally preferred  
5 outcomes in order of importance. Meanwhile, the observer wrote these outcomes on a flipchart  
6 in front of the group.

- 7 - Who would like to share your personally valued outcomes with the group, in order of  
8 importance?  
9 - Could you please clarify why these outcomes of your disease and antirheumatic treatment  
10 are important to you?  
11 - Why did you designate that specific outcome to be the most important?  
12 - Is there anything else you would like to add?

13  
14 *Round 2, step 2: developing a group list of patient-preferred outcomes*

15 The group was asked to generate a consensus list by reviewing and merging all recorded outcomes  
16 and agreeing on the name and properties of each outcome on the list.

- 17 - Could any of the individual expectations be grouped?  
18 - Who would like to suggest a name and meaning for this outcome?  
19 - Do you think all the important outcomes are mentioned on the group list?  
20 - Is there anything else you would like to add?

21 *Round 2, step 3: eliciting personal preferred outcomes*

22 Starting from the consensus list of patient-preferred outcomes that resulted in step 2, each group  
23 member was asked to independently try to select his or her 5 top outcomes from this list, using  
24 the sticky note ordering scheme.

25  
26 *Round 2, step 4: eliciting preferred outcomes in the actual stage of RA*

27 The group was then asked to discuss a collective top 5 outcomes and to consider influencing  
28 factors.

- 29 - Looking at the group list, what outcome would you order as most important?  
30 - What outcome would you order second...fifth?  
31 - Can you tell us why this outcome is either important to you or not?

32 *End of round 2*

33 That is it for the second round. Is there anything else to add?

34 *Round 3: exploring the view of participants on the evolution of their patient-preferred outcomes over*  
35 *the past year*

36 The focus groups ended by exploring the participants' views on potential changes in personally  
37 preferred outcomes over time. During the individual interview of last year, you were asked for  
38 your preferred illness and treatment outcomes. In the meantime, you have gained more  
39 experience with your disease and treatment and the critical disease stage has passed.

- 40 - Do you feel that other results are now more important to you than the ones you identified at  
41 the start or during your interview last year?  
42 - Could you explain why this has or has not changed?  
43 - Are there outcomes that are now more, less, or no longer important to you?  
44 - Why do you think that these are now more or less important than a year ago, or are no longer  
45 important? What may have caused this change in importance?  
46 - Do you have an example of an outcome that has changed in importance compared to that  
47 outcome in the early disease stage? Why do you think this has changed? Could you clarify  
48 this in more detail?  
49 - In general you mention (more or less) similar/different outcomes of importance compared to  
50 last year (in the early disease stage). What is your opinion on this observation?

51  
52 *End of round 3*

53 This is the end of the third round. Is there anything else to add?  
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3 Probing questions: Is this outcome also important or not important to other group members? Are there  
4 any suggestions from other group members? Is there anyone who has a different opinion on the  
5 matter? Is it difficult for you to share your opinion on this? Does everyone agree? Who agrees or  
6 disagrees and why? Who would like to add something?

7 *End of the focus group*

- 8 - What is your general conclusion about today's focus group on preferred and important  
9 outcomes of disease and treatment in the actual disease stage?  
10 - To summarize, you talked about [...]. Do you agree with this summary of today's focus group?

### 11 **Individual interviews at $t_2$**

12 *Preparatory phase (5 to 10 minutes)*

13 Please, consider the next 5 to 10 minutes the question below by writing down as many keywords  
14 as possible. The interviews will begin by discussing your written answers to this question:

- 15 - Which outcomes of your illness and antirheumatic treatment are important to you at this  
16 moment?  
17

18 *Start of the interview*

- 19 - Can you tell me what you have written down? So, which outcomes of your illness and  
20 antirheumatic treatment are important to you at this moment?

21 *Proceeding of the interview*

22 Exploring patient-preferred outcomes

- 23 - How has the treatment been working for you so far?  
24 - To what extent do the expectations you had at the start of your treatment match your current  
25 expectations?  
26

27 Exploring the view of participants on the evolution of their preferred outcomes over the past year

28 Last year, during the interview, you mentioned that the following outcomes of your treatment were  
29 important: ..... ( $t_1$  keywords of the  $t_2$  participant).

- 30 - Do you feel that other results are now more important to you than the ones you identified at  
31 the start or during your interview last year? Could you explain why this has or has not  
32 changed?  
33 - Are there outcomes that are now more, less, or no longer important to you?  
34 - Why do you think that these are now more or less important than a year ago, or are no  
35 longer important? What may have caused this change in importance?  
36 - Do you have an example of an outcome that has changed in importance compared to that  
37 outcome in the early disease stage? Why do you think this has changed? Could you clarify  
38 this in more detail?  
39

40 Patient-preferred outcomes compared to the focus groups at  $t_2$

41 During the focus groups the following 5 treatment outcomes were found to be most important: 1)  
42 preferred outcome; 2) preferred outcome; 3) preferred outcome; 4) preferred outcome; 5)  
43 preferred outcome.

- 44 - I wonder if you recognize yourself in this? Could you explain why this is or is not the case?

45 *End of the individual interview*

46 Is there anything else you would like to add?

47  $t_1$ : time point 1= 3-6 months after start of the initial treatment for early rheumatoid arthritis;

48  $t_2$ : time point 2= 12-18 months after start of the initial treatment for early rheumatoid arthritis.

49 \*Van der Elst K, Meyfroidt S, De Cock D, et al. Unraveling Patient-Preferred Health and Treatment  
50 Outcomes in Early Rheumatoid Arthritis: A Longitudinal Qualitative Study. *Arthritis Care Res (Hoboken)*  
51 2016;68(9):1278-87.  
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**Supplementary file 2** EQPERA Data collection template

<b>Enrollment and interview logistics (<math>t_1</math> and <math>t_2</math>)</b>	
Respondent ID	ID number
Date of birth	dd/mm/yyyy
Gender	man, woman, X
Respondents' place of residence	postal code, location
Responsible recruiter	function, name, contact details
Rheumatology center	name, location
Type of rheumatology center	academic hospital, general hospital, private practice
Treating rheumatologist	name
Date of diagnosis	dd/mm/yyyy
Symptom duration	in months, [date of diagnosis - date of symptom onset]
Disease duration	in months; calculated with date of diagnosis
Comorbidity	no severe comorbidities present [yes/no]
Date of RA treatment initiation	dd/mm/yyyy
Months of treatment experience at $t_1$	date interview $t_1$ - date treatment initiation = between 3-6 months
Initial treatment	the local treatment protocol for early RA: free text, no details on dosages
Initial treatment allocated according to clinical prognostic factors	yes/no
Step-down strategy	yes/no (as initial treatment strategy)
MTX-only step-up	yes/no (as initial treatment strategy)
MTX + early bridging glucocorticoids	yes/no (as initial treatment strategy)
o glucocorticoids starting dose <30mg/day	yes/no
o glucocorticoids starting dose $\geq$ 30mg/day	yes/no
Early combination therapy classical DMARDs with glucocorticoids	yes/no (as initial treatment strategy)
o number of DMARDs included	number
o glucocorticoids starting dose <30mg/day	yes/no
o glucocorticoids starting dose $\geq$ 30mg/day	yes/no
Early combination therapy classical DMARDs without glucocorticoids	yes/no (as initial treatment strategy)
o number of DMARDs included	number
Biologicals as a first hit	yes/no (as initial treatment strategy)
Responder to initial treatment (at moment of $t_1$ recruitment)	yes/no
Patient obliged or deciding to discontinue RA treatment (at moment of $t_1$ recruitment; e.g., because of safety reasons, patient's decision)	yes/no
Reason to not recruit patient	free text or N/A (not applicable)
Date of study invitation	dd/mm/yyyy (sharing of invitation letter)
Reason in case not interested in study (if shared)	free text
Invitation for $t_1$ by phone (if interested)	dd/mm/yyyy (first contact between patient and researchers)

1		
2		
3	Verbal consent for $t_1$ after phone call	yes/no
4	Contact details patient	address/phone number/email
5	Patient-preferred contact method	by phone or email
6	Date and timing of individual interview $t_1$	dd/mm/yyyy; hour
7	Location of individual interview $t_1$	home or rheumatology practice/clinic
8	Reminder for $t_1$ sent	dd/mm/yyyy
9	Reason in case interview $t_1$ was cancelled (if shared)	free text
10	Respondent gave written informed consent $t_1$	yes/no
11	Interviewer $t_1$	name
12	Interviewer is involved as participant's health professional in daily practice	yes/no
13	$t_1$ respondent gave consent at $t_1$ to be contacted again for second part of study ( $t_2$ )	yes/no
14	Reason in case not interested in $t_2$ (at $t_1$ ) participation (if shared)	'Not interested to share own experiences in group', 'Feeling uncomfortable to talk in group', 'Fear for seeing other patients', 'Not interested in the story of other patients', 'Other'
15	Months of treatment experience at $t_2$	date focus group - date treatment start= at least 1 year (between 12-18 months) after treatment initiation
16	Invitation letter $t_2$ sent by post	dd/mm/yyyy (by researchers)
17	Invitation for $t_2$ by phone	dd/mm/yyyy (by researchers)
18	Verbal consent for $t_2$ after phone call	yes/no
19	If not interested in group interview, interested in individual interview instead?	yes/no
20	Reason in case not interested in $t_2$ (if shared)	'Not interested to share own experiences in group', 'Feeling uncomfortable to talk in group', 'Fear for seeing other patients', 'Not interested in the story of other patients', 'Other'
21	Date and timing of focus group $t_2$	dd/mm/yyyy; hour
22	Location of focus group $t_2$	clinical or non-clinical setting
23	If applicable: Date and timing of individual interview $t_2$	dd/mm/yyyy; hour
24	If applicable: Location of individual interview $t_2$	home or rheumatology practice/clinic
25	Reminder for $t_2$ sent (focus group or individual interview)	dd/mm/yyyy
26	Reason in case focus group (or individual interview) $t_2$ was cancelled (if shared)	free text
27	Respondent gave written informed consent $t_2$	yes/no
28	Moderator $t_2$	name
29	Observer(s) $t_2$	name(s)
30	If applicable: Interviewer $t_2$	name
31	Are the (interviewers/) moderators/observers involved as health professionals in the participants' daily clinical care	yes/no
32	<b>Socio-demographic data: patient-reported <math>t_1</math></b>	
33	Date of birth	dd/mm/yyyy
34	Gender	man, woman, X
35	Educational level $t_1$	low, moderate, high
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3	Currently employed $t_1$	yes/no
4	Employment status $t_1$	employed, not employed, retired,
5		housewife/houseman, student
6	Marital status $t_1$	single, together unmarried, married, widower,
7		other
8	Living status $t_1$	alone, with partner and/or kids, with other
9		persons

#### Socio-demographic data: patient-reported $t_2$

11		
12	Educational level $t_2$	low, moderate, high
13		
14	Currently employed $t_2$	yes/no
15	Employment status $t_2$	employed, not employed, retired,
16		housewife/houseman, student
17	Marital status $t_2$	single, together unmarried, married, widower,
18		other
19	Living status $t_2$	alone, with partner and/or kids, with other
20		persons

#### Clinical data: patient-reported data $t_1$

23		
24	VAS general health $t_1$	100-mm visual analogue scale from best (0/100)
25		to worst (100/100)
26	VAS pain $t_1$	100-mm visual analogue scale from best (0/100)
27		to worst (100/100)
28	VAS fatigue $t_1$	100-mm visual analogue scale from best (0/100)
29		to worst (100/100)
30	Key words in preparation of $t_1$ interview	Key words describing:
31		- the impact of RA on their life
32		- which outcomes of their illness and treatment
33		they considered most important

#### Clinical data: patient-reported data $t_2$

35		
36	VAS general health $t_2$	100-mm visual analogue scale from best (0/100)
37		to worst (100/100)
38	VAS pain $t_2$	100-mm visual analogue scale from best (0/100)
39		to worst (100/100)
40	VAS fatigue $t_2$	100-mm visual analogue scale from best (0/100)
41		to worst (100/100)
42	Key words in preparation of $t_2$ focus group	Key words describing which outcomes of their
43	(/interview)	illness and treatment they considered most
44		important

#### Clinical data: health professional-reported data $t_1$ and $t_2$ (to be extracted from database/patient file)

47		
48		
49	Date of diagnosis	dd/mm/yyyy
50	Symptom duration	in months, [date of diagnosis - date of symptom
51		onset]
52	Disease duration	in months; calculated with date of diagnosis
53	Comorbidity	no severe comorbidities present [yes/no]
54	Start of treatment	dd/mm/yyyy
55	Months of treatment experience at $t_1$	date interview $t_1$ - date treatment start = between
56		3-6 months
57	Months of treatment experience at $t_2$	date focus group $t_2$ - date treatment start = at least
58		1 year
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Initial treatment	the local treatment protocol for early RA, free text, no details on dosages
Initial treatment allocated according to clinical prognostic factors	yes/no
Step-down strategy	yes/no (as initial treatment strategy)
MTX-only step-up	yes/no (as initial treatment strategy)
MTX + early bridging glucocorticoids	yes/no (as initial treatment strategy)
○ glucocorticoids starting dose <30mg/day	yes/no
○ glucocorticoids starting dose ≥30mg/day	yes/no
Early combination therapy classical DMARDs with glucocorticoids	yes/no (as initial treatment strategy)
○ number of DMARDs included	number
○ glucocorticoids starting dose <30mg/day	yes/no
○ glucocorticoids starting dose ≥30mg/day	yes/no
Early combination therapy classical DMARDs without glucocorticoids	yes/no (as initial treatment strategy)
○ number of DMARDs included	number
Biologicals as a first hit	yes/no (as initial treatment strategy)
Treatment failure in the first year	yes/no
Treatment failure after 1 year	yes/no
Patient who discontinued treatment ( $t_1$ or $t_2$ ; e.g., because of safety reasons, patient's decision)	yes/no

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*Note.* RA: Rheumatoid Arthritis; MTX: Methotrexate; DMARDs: Disease-Modifying Anti-Rheumatic Drugs; VAS: Visual Analog Scale;  $t_1$ : time point 1= 3-6 months after start of the initial treatment for early rheumatoid arthritis;  $t_2$ : time point 2= 12-18 months after start of the initial treatment for early rheumatoid arthritis.

**Supplementary file 3** EQPERA data quality assurance reporting tool

**Domain 1: Research team and reflexivity**

Item	Guide questions/description
<i>Researcher characteristics</i>	
1. Interviewer / moderator/observer	Who conducted the interviews/ focus groups? (who observed the focus groups?) <ul style="list-style-type: none"> <li>▶ Maximum 2 interviewers at <math>t_1</math> and <math>t_2</math> /country and maximum 1 moderator at <math>t_2</math>/country</li> <li>▶ Preferably the same observer(s) for each focus group</li> </ul>
2. Credentials / background	What were the researcher's credentials? (e.g., PhD, RN)
3. Occupation	What were the researcher's occupation at the time of the study?
4. Gender	Was the researcher male or female?
5. Experience and training	What experience or training did the researcher have?
<i>Relationship with participants</i>	
6. Relationship established	Was a relationship established prior to study commencements? (e.g., health professional)
7. Participant knowledge of the interviewer	What did the participant know about the researcher? (e.g., personal goals, reasons for doing the research)
8. Interviewer characteristics	What characteristics were reported about the interviewer/moderator/observer? (e.g., bias, assumptions, reasons and interest in the research topic)

**Domain 2: Study design (a longitudinal, qualitative, explorative study)**

<i>Participant selection</i>	
9. Sampling	How were participants selected (e.g., purposively) Mono or multicenter sampling? Type of recruitment center(s)? (i.e., academic hospital, general hospital or private practice)
10. Method of approach	Who invited the participants? How were participants approached? (e.g., face to face, telephone, mail, email)
11. Sample size	How many participants were in the study? <ul style="list-style-type: none"> <li>◆at <math>t_1</math>: number of individual interviews</li> <li>◆at <math>t_2</math>: number of participants per focus group / number of individual interviews</li> </ul>
12. Non-participation	How many eligible patients could potentially be recruited? How many people were approached and how many of them refused to participate or dropped out? Reasons? (if shared) <ul style="list-style-type: none"> <li>◆Not interested in participation (refusal)</li> <li>◆Drop out (type 1): in case <math>t_1</math> interview was scheduled and cancelled</li> <li>◆Not interested in participation at <math>t_2</math> (drop out, type 2)</li> <li>◆Not interested in participation in a focus group, but willing to participate in an individual interview instead at <math>t_2</math></li> <li>◆Drop out (type 3): in case <math>t_2</math> interview was scheduled and cancelled</li> </ul>

*Setting*

13. Setting of data collection Where was the data collected?
14. Presence of non-participants Was anyone else present besides the participant and researchers?
15. Description of sample What are the important characteristics of the sample? (e.g., demographic data)

*Data collection*

16. Interview guide Were questions, prompts, guides provided by the authors?  
Was the interview guide pilot tested?  
Is it being made available?
17. Focus group guide Were questions, prompts, guides provided by the authors?  
Was the interview guide pilot tested?  
Is it being made available?
18. Audio / visual recording Did the research use audio or visual recording to collect the data?
19. Data collection method How were the data collected? ( $t_1$ : focus group or individual interview?)  
Were repeat interviews carried out at  $t_2$ ?
20. Field notes Were field notes made during and/ or after the interview or focus group?  
► if yes, please record them in the descriptive or methodological interview report.  
Were short reports prepared after each interview?
21. Duration What was the duration of the interviews or focus groups?
22. Data saturation Was data saturation discussed?  
After how many interviews was data saturation reached? (Definition in EQPERA: "if the last 3 interviews do not provide new information, insights or additional understanding to accomplish the study aims")

**Domain 3: Analysis and findings***Data analysis*

23. Number of data coders How many data coders coded the data?  
Who coded the data?
24. Independent coding Was the analysis repeated by more than 1 researcher to ensure reliability?
25. Data analysis method How were themes and concepts identified from the data? (e.g., Were themes identified in advance (framework-based) or derived from the data (data-driven?)
26. Patient research partners Did patient research partners provide feedback on the findings, and in which part(s) of the data analysis were they involved?
27. Software What software was used to manage the data?

*Reporting*

28. Quotations presented Were participant quotations presented to illustrate the themes/findings?  
Was each quote identified? (e.g., participant number, gender, age)
29. Data and findings consistent Was there consistency between the data presented and the findings?
30. Clarity of themes Were themes clearly presented in the findings?

## Domain 4: Data management strategies

### *Data recording*

31. Recording changes and decisions  
Were changes to the interview guide, the evolution in themes, deviations from the research protocol, and major local project decisions carefully documented along with the rationale for change?
- ▶ to recall decisions
  - ▶ the use of a research log book is recommended
32. Recording interview data  
Did you record the data with at least 2 audio recorders?
- ▶ to prevent missing data

### *Data storing*

33. Routinely storing of data  
Was the data (e.g., audio files, transcripts, interview reports and field notes, patient-reported and clinical data, informed consents) or the project database routinely submitted to a central data repository or a secured cloud storage system?
- ▶ to avoid missing data and to easily manage large amounts of data like in qualitative research
  - ▶ a uniform transcript header and file name could facilitate data storing (e.g., T1.number of interview.ddmmyyyy.initials of interviewer)

### *Data check*

34. Internal audit  
Could the evidence (field notes, interview transcripts, recordings, reasons for interview guide adaptations,...) be inspected by others?
35. Preventing missing data  
Did the principal investigator routinely check for missing data?

### *Data collection*

36. Recruitment flow  
Was the recruitment flow carefully documented?
- ▶ the use a research log book (enrollment spread sheet) is suggested
37. Templates  
Did you check the data collection templates and the Excel spread sheet?
38. Local interview guide  
Translation/cultural adaptation interview guide:  
Did you use the proposed framework to translate the interview guide into the source language?  
Were cultural adaptations needed?
- ▶ please, record these in your research log book, together with the timing and the reason for adjustment
39. Avoiding and handling the presence of a third person  
Focus of attention during interview scheduling:  
Was the purpose of a one to one interview mentioned to the participant?  
If someone else was present, did this affect the interview/data collection?
- ▶ please, reflect on this in the descriptive interview report
40. Introducing the interview  
Did you prepare and practice the interview introduction?
- ▶ to maximize the interview return
  - ▶ key words: welcoming the participant; introducing yourself; clarifying the purpose and importance of research, the importance of participant contribution, expectations regarding the participant (e.g., no good or wrong answers), role of the interviewer/moderator/observer, (t<sub>2</sub>: “rules” regarding group discussion), ethical aspects; “Any questions?”; mobile phone on silent mode)

- 1  
2  
3 41. Interview burden It is recommended to conduct 1 individual interview/day, with a maximum of  
4 2 interviews/day  
5 ▶ to avoid interview burden and to have sufficient time to reflect on each  
6 interview  
7  
8 42. Interview reports Did you write for each interview/focus group 3 short reports? (i.e., content  
9 report, descriptive report, methodological report)  
10  
11 43. Iterative process Did you use an iterative process of data collection and analysis?  
12 ▶ to support data saturation

### *Data analysis*

- 13  
14 44. Analysis guide Did you use Qualitative Analysis Guide of Leuven (QUAGOL) to guide your  
15 data analysis?  
16 Did you use Saldaña's guiding questions for analyzing the longitudinal  
17 data?  
18  
19 45. Peer debriefings Were regular peer debriefings held?  
20 ▶ time for reflection (in team): to discuss the interview return, the  
21 development of new themes, and to question and confirm saturation of  
22 themes  
23 ▶ early in de coding and interviewing process, more frequent meetings  
24 are suggested  
25 ▶ please make a short report of each debriefing to recall discussions  
26  
27 46. Team analysis Was looked at the data in team (from different perspectives looking at the  
28 data)  
29

### *Transcription*

- 30  
31 47. Transcription Who transcribed the data?  
32 guidelines  
33 ▶ >1 person: did you apply a uniform transcription method? (e.g.,  
34 agreements about the level of details, to obtain confidentially, to  
35 reproduce the exact words spoken)  
36 ▶ external transcriber: was the interview transcript reviewed by the  
37 interviewer on data quality and accuracy of transcribing? How did you  
38 approach this quality check?  
39

### *Team approach*

- 40  
41 48. Patient research What was the exact role of the patient research partners in the study  
42 partners  
43  
44 49. Interdisciplinary Who joined the interdisciplinary team, and what was their contribution?  
45 team  
46

### *Initiation session*

- 47  
48 50. Project initiation Did the local research team (at least the principal investigator) followed the  
49 initiation session lead by the project leader at  $t_1$  and at  $t_2$ ?

50  
51  $t_1$ : time point 1= 3-6 months after start of the initial treatment for early rheumatoid arthritis;  $t_2$ : time point  
52 2= 12-18 months after start of the initial treatment for early rheumatoid arthritis.  
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