PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	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
AUTHORS	Van der Elst, Kristien; Bremander, Ann; De Groef, An; Larsson, Ingrid; Mathijssen, Elke; Vriezekolk, J; Westhovens, Rene; van Eijk-Hustings, Yvonne

VERSION 1 – REVIEW

REVIEWER	Professor Hania Salah Zayed Rheumatology and Rehabilitation Department, Faculty of Medicine, Cairo University Egypt
REVIEW RETURNED	06-May-2018

GENERAL COMMENTS	Methods and Analysis: Patient recruitment has already started in The Netherlands and Sweden. What is the anticipated time for termination of this study? "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 .." Comment: - It has not been explained why the socio-demographic information was obtained before the interview and the visual analog scales for assessment of general health, pain and fatigue were obtained after the interview i.e. at two separate time points. -Will this information be obtained at the interview at t2 only (although the subheading is "Procedures at both time points"? Please clarify. -No details have been mentioned regarding the type of clinical information that will be extracted from the medical records e.g. laboratory data, disease activity scores, functional assessment scores.

REVIEWER	Betty Hsiao Yale University School of Medicine, United States
REVIEW RETURNED	15-Sep-2018

GENERAL COMMENTS	Firstly, thank you for sharing this protocol. I welcome studies that help us more clearly understand how to treat patients with rheumatoid arthritis from their perspectives and the use of qualitative research techniques will be helpful in that respect. As local context may influence treatment and outcome preferences, I also agree that it is important to see how perspectives vary among different countries, *i.e.* if perspectives converge or differ from the original Belgian study. I have a few comments about this protocol: 1) In regards to recruitment and patient sampling: a. The protocol states that patients will be recruited from multiple centers across different geographic locations and will be sampled based on their age/life phase, gender, and treatment progress/treatment experience. How will the authors take into account varying levels of health literacy? b. The authors state that sociodemographic data will also be collected in addition to patients reporting on their general health, level of pain and fatigue. Will the authors be asking about the level of disability or work absenteeism? This information may be helpful as part of the analysis as well. 2) I understand that data will be collected by the local teams and then coded by the local teams prior to being combined for EQPERA purposes—while I understand the logistics and concern for feasibility, is this a possible limitation, *i.e.* that there are different teams evaluating the original transcripts?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Response: We thank Professor Hania Salah Zayed for reviewing our manuscript.

Methods and Analysis:

Query 1: Patient recruitment has already started in The Netherlands and Sweden. What is the anticipated time for termination of this study?

Response: This information could indeed be of interest to the readers and is now added to the manuscript.

Page 6 , original: Start of patient inclusion was 2016 in The Netherlands and 2017 in Sweden.

→ **Added on page 6:** Start of patient inclusion was 2016 in The Netherlands and 2017 in Sweden. We intend to publish the final results by the end of 2019.

Query 2: "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 .."

Query 2a: It has not been explained why the socio-demographic information was obtained before the interview and the visual analog scales for assessment of general health, pain and fatigue were obtained after the interview i.e. at two separate time points.

Response: Thank you for this good remark. The collection of the visual analog scales after the interviews was purposively chosen to not influence patient opinion about outcome preferences. This is now added to the manuscript.

Þ Page 13, original: 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.

→ Added on page 13: Prior to the (focus group) interview, participants will document socio-demographic information. They will report about their general health, level of pain and fatigue during the past week on a visual analog scale after the interviews to avoid influencing patient opinion in advance.

Query 2b: Will this information be obtained at the interview at t2 only (although the subheading is "Procedures at both time points"? Please clarify.

Response: We understand this remark and adjusted the sentence accordingly.

Þ Page 13, original:

VERSION 2 – REVIEW

REVIEWER	Professor Hania Salah Zayed Rheumatology and Rehabilitation Department, Faculty of Medicine, Cairo University Cairo, Egypt
REVIEW RETURNED	18-Oct-2018

GENERAL COMMENTS	Comments: Thank you for doing the amendments in the revised version of the manuscript, however, addressing the comments below would add more clarity and improve the outlook of your manuscript. Figure 2: Please mention the language of the original interview guide which is translated, is it Belgian or English? If the language is Belgian, it is not clear why the source language is English? Supplementary file 2: - The section on enrollment and interview logistics (t1 and t2) contains questions that are also mentioned in the section: “Clinical data: health professional-reported data t1 and t2 (to be extracted from database/patient file)” e.g. symptom duration, disease duration, details of treatment and clinical response. Is there a need for this repetition? - No definition has been given for “severe comorbidity”.

REVIEWER	Betty Hsiao Yale University School of Medicine
REVIEW RETURNED	03-Nov-2018

GENERAL COMMENTS	Thank you sharing this study design on such an important issue.

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Comment: Thank you for doing the amendments in the revised version of the manuscript, however, addressing the comments below would add more clarity and improve the outlook of your manuscript.
Response: We thank Professor Zayed for reviewing our revised manuscript and providing us with additional comments to improve the clarity of the manuscript. Please, find our responses below.

Query 1: Figure 2: Please mention the language of the original interview guide which is translated, is it Belgian or English? If the language is Belgian, it is not clear why the source language is English?

Response: English is the project language in EQPERA, because the Swedish research team does not understand the Flemish and (related) Dutch language. To this end, the original interview guide in the Flemish language was first translated into English, and this English version was then used as a source for the forward-backward translation from English into Swedish. We clarified this in the manuscript on page 11. The framework that we used for translation of the interview guides is explained in figure 2, with the translation from English into Swedish as an example. Referring to other literature, the English version was used as the source version for the translation into the target language (i.e., Swedish).

Page 11, original: 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 to English and Swedish (Figure 2).40 41

→ **Added on page 11**: 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 in Figure 2.[40 41]

Query 2: Supplementary file 2:

2a: The section on enrollment and interview logistics (t1 and t2) contains questions that are also mentioned in the section: “Clinical data: health professional-reported data t1 and t2 (to be extracted from database/patient file)” e.g. symptom duration, disease duration, details of treatment and clinical response. Is there a need for this repetition?

Response: We appreciate the reviewer for reviewing this supplementary file in detail and noticing the repetition. Perhaps, this repetition was not necessary, but it aimed to assist the local teams in considering all relevant variables at recruitment. Supplementary file 2 contains our project files, as the local teams are actively using these while conducting their study, we prefer to not make any changes.

2b: No definition has been given for “severe comorbidity”.

Response: Thank you for this remark. After team discussion, we agreed that patients cannot be included in case they have acute/severe comorbidities such as a heart attack. We wanted to interview patients for which RA was the disease of focus and to exclude those for which other diseases or health problems were playing a more prominent role in their lives. This to have accurate responses to our central research question on patient-preferred outcomes in early RA. Supplementary file 2

contains our project files, as the local teams use them actively while conducting their study, we prefer to not make any changes.

Reviewer: 2

Comment: Thank you sharing this study design on such an important issue.