BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (http://bmjopen.bmj.com/site/about/resources/checklist.pdf) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

**TITLE (PROVISIONAL)**
Approaches to improving symptom appraisal: a systematic literature review

**AUTHORS**
Xiang, Ling; Yoon, Sungwon; Low, Andrea; Leung, Ying Ying; Fong, Warren; Lau, Tang Ching; Koh, Dow Rhoon; Thumboo, Julian

### VERSION 1 – REVIEW

**REVIEWER**
Simone Parisi  
Azienda Ospedaliero Universitaria Città della Salute e della Scienza di Torino, RHEUMATOLOGY

**REVIEW RETURNED**
04-Jan-2022

**GENERAL COMMENTS**

Dear Author,
I have read your review carefully concerning symptom appraisal in patients with ARDs
The review is complete and deals with interesting aspects.
I have some suggestions for some points to review:
- Methods: was the research carried out by multiple authors? How was the quality of the selected works assessed (for example with Method Agree II)?
  
  It would be appropriate to add an assessment on the quality of the studies on the risk of bias (e.g. Grade System).
- Discussion: the discussion is very long and there are some concepts repeated several times. Furthermore, some descriptions (for example the Raynaud phenomenon) could be omitted to make the discussion more fluid. I would suggest focusing the discussion better and shortening it.

Tables: table 1 does not indicate the acronym "Nil"; table 2 is unclear, a complete caption should be included, please indicate the measurement units (n, %)

Prisma: in "Records excluded (n = 10,412) indicate" why? "

Best Regards

**REVIEWER**
Elisabet Welin  
Orebro Universitet, School of Health Sciences

**REVIEW RETURNED**
21-Mar-2022

**GENERAL COMMENTS**

This paper addresses an interesting and relevant topic: symptom appraisal in pre-disease or early disease could potentially be important tools for diagnosis. However, in it's present form, this paper needs to be tightened and more focused.
Comments on various points in the review checklist:
1) The title is misleading: this is more of a general literature review of symptom appraisal (contains only 2 articles on ARD). Symptom appraisal is interesting and relevant in itself, the content should be clear when reading the title.
The authors argue short but well for the relevance of symptom appraisal and thus this literature review. The aim/research question however includes the ambition to construct a framework for symptom appraisal, which is not argued for
2) The abstract does not fully correspond to the conclusions drawn in the article
4) Relevant and well performed methodology, but needs a clarification on the choice of used keywords as well as the consequences of possible bad indexing when it is (like in this case) not possible to use MeSH-terms
6) Outcomes need to be more clear, it is now a bit woobly between ARD and a more general approach
9) Since the objective is yet unclear (see above), the answer is also unclear. However, the results are presented in a comprehensible way and if the authors chose a more focused approach, the results could be of distinct interest.
11) The discussion is extremely long, and has a main focus on the presentation of an integrated conceptual framework. If that is to be the important outcome, this has to be much more paved for in the article.
12) Study limitations do not include any discussion on methodological issues, i.e. the choice and use of key words, and the risk of missing relevant articles due to this.

As a concluding remark: there is a lot to learn on symptom appraisal, and this article has the potential to address issues of great interest. As for now, when the title does not correspond to the objective, and later in the article when a conceptual framework is proposed without having been anchored, the article seems a bit unfinished and would benefit of a more focused approach.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Dr. Simone Parisi, Azienda Ospedaliero Universitaria Città della Salute e della Scienza di Torino

Comments to the Author:

Dear Author,
I have read your review carefully concerning symptom appraisal in patients with ARDs
The review is complete and deals with interesting aspects.
I have some suggestions for some points to review:

Comment 1:
- Methods: was the research carried out by multiple authors? How was the quality of the selected works assessed (for example with Method Agree II)? It would be appropriate to add an assessment on the quality of the studies on the risk of bias (e.g. Grade System).

Reply 1:
This research was conceptualized by all authors while the literature screening, quality assessment and data extraction were carried out primarily by the first author (as part of her PhD training), with any uncertainty resolved by discussion with the other authors. We have added this in the methods.
We screened the title and abstract of all articles identified from the final literature search.

One main reviewer (the first author) screened the title and abstract of all articles identified from the final literature search, with any uncertainty resolved by discussion with the other authors.

We have also added in other necessary details in the revised manuscript according to the PRISMA checklist as suggested by Handling editor (see Comment 15). We are open to publishing this literature review as a systematized review if 2 or more reviewer are required for systematic reviews.

The quality of selected articles was checked using the JBI critical appraisal tools and the details of quality assessment have been added in the methods and results sections.

Original methods:
Nil

Revised methods:
Quality assessment was conducted using the Joanna Briggs Institute (JBI) critical appraisal tools primarily by the first author, with any uncertainty resolved by discussion with the other authors (1, 2).

Original results:
Nil

Revised results:
Of these 29 studies, 13 were categorized as having low risk of bias (3-15), 10 were categorized as having moderate risk of bias (16-25), and 6 were unable to be assessed due to a lack of detailed evaluation of the developed approaches (26-31). We included all 29 studies in the synthesis as our focus was the development instead of the evaluation of approaches.

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1 Systematized reviews attempt to include one or more elements of the systematic review process while stopping short of claiming that the resultant output is a systematic review. Systematized reviews are typically conducted as a postgraduate student assignment, in recognition that they are not able to draw upon the resources required for a full systematic review (such as two reviewers). From Grant, M. J. and Booth, A. (2009), A typology of reviews: an analysis of 14 review types and associated methodologies. Health Information & Libraries Journal, 26: 91-108. doi:10.1111/j.1471-1842.2009.00848.x
**Comment 2:**
Discussion: the discussion is very long and there are some concepts repeated several times. Furthermore, some descriptions (for example the raynaud phenomenon) could be omitted to make the discussion more fluid. I would suggest focusing the discussion better and shortening it.

**Reply 2:**
We thank Reviewer 1 for the helpful suggestion. We have shortened the discussion by removing repeated concepts and the illustration of how proposed framework could be incorporated into the development of a screening tool for ARDs, the latter was presented as a supplementary file instead.

**Comment 3:**
Tables: table 1 does not indicate the acronym "Nil"; table 2 is unclear, a complete caption should be included, please indicate the measurement units (n, %)

**Reply 3:**
We have added an explanation for "Nil" in the footnote of Table 1, and revised the caption and added measurement units in Table 2.

Original Table 1 footnote:
Nil

Revised Table 1 footnote:
Nil: no theories/models were adopted

Original Table 2 caption:
Characteristics of approaches included in the synthesis

Revised Table 2 caption:
Characteristics of approaches developed for various health conditions

**Comment 4:**
Prisma: in "Records excluded (n = 10,412) indicate" why? 

**Reply 4:**
Records were excluded based on the pre-defined inclusion and exclusion criteria. We have added the reasons for exclusion of these records in the PRISMA chart.

Original:

Revised:
Best Regards

Reviewer: 2
Prof. Elisabet Welin, Orebro Universitet

Comments to the Author:

Comment 5:
This paper addresses an interesting and relevant topic: symptom appraisal in pre-disease or early disease could potentially be important tools for diagnosis. However, in it's present form, this paper needs to be tightened and more focused.

Reply 5:
We thank Reviewer 2 for highlighting the significance of this research. Indeed, symptom appraisal is an important process that could be targeted to facilitate early diagnosis. We have removed the redundant parts to make the revised manuscript tightened and more focused, as detailed below.

Comments on various points in the review checklist:
Comment 6:
1) The title is misleading: this is more of a general literature review of symptom appraisal (contains only 2 articles on ARD). Symptom appraisal is interesting and relevant in itself, the content should be clear when reading the title. The authors argue short but well for the relevance of symptom appraisal and thus this literature review. The aim/research question however includes the ambition to construct a framework for symptom appraisal, which is not argued for

Reply 6:
We have revised the title to better reflect the scope of literature review and added in justifications for constructing a framework for symptom appraisal in the objectives.

Original title:
Approaches to Improving Symptom Appraisal in Patients with Autoimmune Rheumatic Diseases: A Literature Review

Revised title:
Approaches to Improving Symptom Appraisal: A Systematic Literature Review

Original objectives:
Poor symptom appraisal (detection, interpretation and response to symptoms) plays a major role in prolonged pre-diagnosis interval in autoimmune rheumatic diseases (ARDs), an unmet need worldwide. We therefore aimed to review existing approaches to improving symptom appraisal in the literature.

Revised objectives:
Poor symptom appraisal (detection, interpretation and response to symptoms) plays a major role in prolonged pre-diagnosis interval in various health conditions such as cancer and autoimmune rheumatic diseases (ARDs). Theories and models have been proposed to study the symptom appraisal process but how they could be employed to improve symptom appraisal remains unclear. We therefore aimed to review approaches to improving symptom appraisal in the literature and to develop a theoretical framework that could guide the development of approaches to improving symptom appraisal among individuals in the general population to facilitate early diagnosis.

Comment 7:
2) The abstract does not fully correspond to the conclusions drawn in the article

Reply 7:
We have revised the conclusions to align better with the study objectives and findings.

Original:

Symptom appraisal is an essential process in a patient’s journey that can be targeted to facilitate early diagnosis of ARDs but is largely unstudied. This review provides an insight into the development of approaches to improving symptom appraisal, which could facilitate early identification of ARDs and other health conditions in the general population.

Revised:

Symptom appraisal is an essential process in a patient’s journey that can be targeted to facilitate early diagnosis but is largely unstudied. Building on the literature, we propose a theoretical framework and approaches to improving symptom appraisal. This could facilitate early identification of a variety of health conditions in the general population.

Comment 8:

4) Relevant and well performed methodology, but needs a clarification on the choice of used keywords as well as the consequences of possible bad indexing when it is (like in this case) not possible to use MeSH-terms

Reply 8:

We have added in clarifications on the choice of keywords and have added the possible consequences as one of the limitations in the discussion.

Original:

Nil

Revised:

(study limitations) First, only free-text search was conducted in Web of Science and Scopus due to a lack of controlled vocabularies in these two databases. However, in consultation with a medical librarian with expertise in literature searches, a list of comprehensive free-text search terms were developed based on a preliminary literature search and both controlled vocabulary search and free-text search were used in other databases (Medline, PsycInfo, Embase and CINAHL), which would be sufficient to identify most of the important articles in the literature.

Comment 9:
6) Outcomes need to be more clear, it is now a bit woobly between ARD and a more general approach

Reply 9:
We thank Reviewer 2 for highlighting this issue. Our initial intent was to search for approaches to improving symptom appraisal among patients with ARDs but this yielded a small number of publications that were insufficient to provide a solid basis for developing a theoretical framework and approaches to improving symptom appraisal. We thus expanded our search to all health conditions and found that symptom appraisal was actually an universal unmet need. The theoretical framework we proposed was based on a synthesis of approaches developed for patients with various health conditions, and could thus be adopted in different contexts. We have revised the study title and objective to reflect a more general approach. We have presented the illustration of how the proposed framework could be adopted in the development of screening tools for ARDs as a supplementary file instead. Please refer to the response to Reply 6 for details of revisions to the title and abstract which reflect this.

Comment 10:
9) Since the objective is yet unclear (see above), the answer is also unclear. However, the results are presented in a comprehensible way and if the authors chose a more focused approach, the results could be of distinct interest.

Reply 10:
We have revised the objectives to align better with the results, as detailed in Reply 6.

Comment 11:
11) The discussion is extremely long, and has a main focus on the presentation of an integrated conceptual framework. If that is to be the important outcome, this has to be much more paved for in the article.

Reply 11:
We have removed redundant content and shortened the discussion significantly, as detailed in Reply 2. We have also added in justifications of the integrated conceptual framework, as detailed in Reply 6.

Comment 12:
12) Study limitations do not include any discussion on methodological issues, i.e. the choice and use of key words, and the risk of missing relevant articles due to this.

Reply 12:
We have added a limitation regarding the methodological issues, as detailed in Reply 8.
Comment 13:
As a concluding remark: there is a lot to learn on symptom appraisal, and this article has the potential to address issues of great interest. As for now, when the title does not correspond to the objective, and later in the article when a conceptual framework is proposed without having been anchored, the article seems a bit unfinished and would benefit of a more focused approach.

Reply 13:
We thank Reviewer 2 for the insightful comments. We have revised the title, objectives and discussions in the revised manuscript (as detailed in the replies to comments 6, 7, 9 and 10) to make it congruous and succinct.

Association Editor:

Comment 14:
*I generally share all of Welin’s concerns. It’s also not clear how many authors carried out screening and data extraction. The title is entirely misleading as this ends up being a generic review on approaches to improving symptom appraisal regardless of the condition. Needs to be tightened up and refocused as Welin suggests and include the quality assessment.

Reply 14:
We thank Association Editor for highlighting these concerns. The screening and data extraction was conducted by the first author, with discussions with the other authors for any uncertainty, as detailed in Reply 1. We have revised the title and the content of manuscripts according to both reviewers’ suggestions, as detailed above.

Handling Editor:

Comment 15:
*The authors should include a copy of the PRISMA checklist indicating the page/line numbers of your manuscript where the relevant information can be found (https://imsva91-ctp.trendmicro.com:443/wis/clicktime/v1/query?url=http%3a%2f%2fwww.prisma%2dstatement.org%2f&umid=3AF27D2B-DD13-4905-B245-BA121E68E38E&auth=6e3fe59570831a389716849e93b5d483c90c3fe4-d1a9eaaa17ccee9313fbc2c876ed6fe83c45a496), updating the manuscript to ensure all reporting requirements are met.

Reply 15:
We have included the PRISMA checklist as a supplementary file and reported necessary details in the revised manuscript.
**Comment 16:**
*Relatedly, the title, abstract, and main text should be adjusted to indicate that the manuscript is a systematic review. Note that BMJ Open does not publish narrative literature reviews.*

**Reply 16:**
We thank Handling Editor for highlighting this. We have revised the manuscript to align with the journal requirements.

**Comment 17:**
*Relatedly, the abstract should be reformatted so that it includes the following sections: Objectives >> Design >> Data Sources >> Eligibility Criteria >> Data extraction and synthesis >> Results >> Conclusions. (Eg, https://imsva91-ctp.trendmicro.com:443/wis/clicktime/v1/query?url=http%3a%2f%2fbmjopen.bmj.com%2fcontent%2f8%2f3%2fe019438&umid=3AF27D2B-DD13-4905-B245-BA121E68E38E&auth=6e3fe59570831a389716849e93b5d483c90c3fe4-29fed151b62d497399ee1979261054f5df500e5).*

**Reply 17:**
We have revised the structure of the abstract to align with the journal requirements.

**Comment 18:**
*The authors should clarify if they performed any quality assessment or risk of bias assessment. If so, the details of this should be included in the Methods and Results sections.*

**Reply 18:**
We have added in the details of quality assessment in the revised manuscript, as detailed in Reply 1.

### VERSION 2 – REVIEW

| REVIEWER | Simone Parisi  
|   | Azienda Ospedaliero Universitaria Città della Salute e della Scienza di Torino, RHEUMATOLOGY |
| REVIEW RETURNED | 13-Jun-2022 |
| GENERAL COMMENTS | Dear Author, the changes made are correct, no other comments from my side |
| REVIEWER | Elisabet Welin  
|   | Orebro Universitet, School of Health Sciences |
| REVIEW RETURNED | 20-Jun-2022 |
| GENERAL COMMENTS | In the revised version, the authors have suitably considered and revised according to all my comments. The article is now condensed and cohesive, and I assess it to be of relevance and interest for the scientific community. |