

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Assessing research methodologies used to evaluate inequalities in end-of-life cancer care research: a scoping review protocol
AUTHORS	Davis, Laura; Webber, Colleen; Datta, Geetanjali D.; Wiens, Allison; Harper, Sam; Hallet, Julie; Coburn, Natalie G.; Konikoff, Lauren; Tanuseputro, Peter; Mahar, Alyson

VERSION 1 – REVIEW

REVIEWER	Cotterill, Sarah University of Manchester, Centre for Biostatistics
REVIEW RETURNED	11-Apr-2022

GENERAL COMMENTS	<p>The paper sets out to review literature on health inequities in end-of-life cancer care, to assess whether the study design and methodology are appropriate. This is an important line of enquiry, but it is a complicated review to undertake because the review needs to identify multiple types of study, and many of the included studies may not have inequality or inequity as their primary purpose. The authors have tried to address those issues, but unfortunately the paper has some major flaws which cannot be changed, (assuming the review is already underway):</p> <ul style="list-style-type: none">• The two terms ‘health inequality’ and ‘health inequity’ are central to the review, yet both the definition and the operationalisation of these terms are imprecise. The authors define both terms in the Introduction, but the referencing is inexact and it is unclear whether there has been a comprehensive review of the literature. For example, there are no citations for the definition of health inequality, ‘defined as measured differences in the health or healthcare of individuals and groups’ (p4, line11-12). The definition of health inequity is drawn from 2 references, leaving the reader unclear whether this is a widely held definition. The Introduction includes a statement ‘stigma, bias and structural racism all contribute to health inequities’ (p4 line15-16) and lists some characteristics of subgroups who may experience health inequities as ‘race, ethnicity, gender, sex, religion and socioeconomic status’ (p4 line 23). Neither of these statements include any references to wider literature.• The term health inequity is not clearly operationalised in the review. I would expect the aims, inclusion criteria and search terms to be directed towards a list of sub-groups and possibly also towards a list of inequality types (eg stigma, bias), but I didn’t find that clearly set out. The search itself is very broad in its definition and uses a subject filter for ‘health disparities’, without any explanation of how that term relates to health inequity or health inequality. In the text the search is loosely described as covering terms ‘such as race, sexual orientation, geography etc’, which is different to the list in the Introduction (see above).
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	<ul style="list-style-type: none"> • The list of ‘research questions’ (p5) is a mix of questions and objectives. A number of topics are loosely raised, including: <ul style="list-style-type: none"> o ‘Measures and statistical methods’ used to evaluate end-of-life cancer care inequalities. ‘Measures’ is not defined, making it unclear whether the review will extract cancer care outcome measures or measures of inequity or measures to describe population sub-groups (eg ethnic or gender categories). Later this is expanded to include ‘study design, measures and statistical and analytical techniques’. o How the methods used in the papers ‘align with recommended approaches for studying health inequalities such as ... use of a conceptual framework; consideration of intersectionality and appropriate analytic techniques’. Although this is listed as an aim, and is highlighted in the introduction, it is not operationalised in the methods: the data extraction section does not list conceptual framework or intersectionality as items to be extracted, and there is no list of ‘recommended approaches’ that the data will be compared to. o ‘Gaps in methodology and areas for improvement in future studies’. Identification of gaps in methodology would need a different review, of methodological literature. I feel the paper would benefit from the following amendments: <ul style="list-style-type: none"> • The list of keywords could be strengthened by the addition of terms such as inequalities, protocol, scoping review. • The term ‘equity stratifiers’ needs to be defined at first use. • Add the number of papers found after removal of duplicates (6p line 8). • Add the important dates for the review, either actual or anticipated (eg start date, search date, completion of data extraction). • Inclusion of the data charting table as an appendix. • Mention of bias is currently included in the data extraction section: if bias is to be considered, it would be more appropriate in a separate ‘Risk of bias’ section of the protocol, with a description of how that will be assessed. • Data extraction include the ‘results’. Many of the studies in the review may not have health inequity as their main purpose, so the primary results might not be of interest to this review. There is a need for a clear definition of which results the review will extract. • Provide an explanation of why no patients or public were involved in the review, given how relevant this topic is to patients. • The protocol is not written using any reporting guidelines. If there are no reporting guidelines for scoping reviews, perhaps the reporting guideline for systematic reviews could be adapted for this purpose: Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. Syst Rev. 2015;4(1):1. doi: 10.1186/2046-4053-4-1. • The review will include both qualitative and quantitative papers, but throughout the paper more attention is given to the quantitative papers, and there is insufficient description of how the qualitative papers will be dealt with at each stage of the review. • The three broad categories of search terms are described in the Methods section as cancer, end-of-life and health inequalities. Yet, in the Medline search, ‘cancer’ only appears as an AND term with ‘end-of-life’, so the search will have identified many end-of life studies outside of cancer, which will not be relevant for the review.
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REVIEWER	Carey, Matthew
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	Churchill Hospital, Palliative Medicine
REVIEW RETURNED	15-Apr-2022

GENERAL COMMENTS	<p>A few notes: Page 4, lines 29-34 - the sentence is very long and difficult to follow, please consider splitting to make easier to read and understand.</p> <p>Overall this is a good summary of the protocol to be used to answer the question regarding inequalities in outcomes for end of life care in cancer patients. I look forward to reading the results in the future.</p>
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VERSION 1 – AUTHOR RESPONSE

Response to Reviewers
bmjopen-2022-062825

We thank the reviewers for their time and feedback on our scoping review protocol entitled “Assessing research methodologies used to evaluate inequalities in end-of-life cancer care research: A scoping review protocol.” We have provided a point-by-point response to each of the reviewer comments below.

Reviewer: 1 Dr. Sarah Cotterill, University of Manchester
Comments to the Author:

The paper sets out to review literature on health inequities in end-of-life cancer care, to assess whether the study design and methodology are appropriate. This is an important line of enquiry, but it is a complicated review to undertake because the review needs to identify multiple types of study, and many of the included studies may not have inequality or inequity as their primary purpose. The authors have tried to address those issues, but unfortunately the paper has some major flaws which cannot be changed, (assuming the review is already underway):

Response: We agree that this scoping review takes on a complicated topic and as such will be challenging. However, much work addressing inequity is complex and does require careful thought and execution. It is not a reason to leave an area unstudied or unevaluated in the literature. We would like to clarify that this scoping review is not yet underway, which was indicated in the submission cover letter. This review is in the planning phase and our intention is to incorporate peer review comments to the protocol in order to improve the quality of the review. As such, we thank the reviewer for their detailed comments. We are confident that we have addressed all of the reviewer’s comments, many of which were focused on the clarity of the manuscript rather than identifying methodological flaws in the planned study design.

- The two terms ‘health inequality’ and ‘health inequity’ are central to the review, yet both the definition and the operationalisation of these terms are imprecise. The authors define both terms in the Introduction, but the referencing is inexact and it is unclear whether there has been a comprehensive review of the literature. For example, there are no citations for the definition of health inequality, ‘defined as measured differences in the health or healthcare of individuals and groups’ (p4, line11-12). The definition of health inequity is drawn from 2 references, leaving the reader unclear whether this is a widely held definition. The Introduction includes a statement ‘stigma, bias and structural racism all contribute to health inequities’ (p4 line15-16) and lists some characteristics of

subgroups who may experience health inequities as ‘race, ethnicity, gender, sex, religion and socioeconomic status’ (p4 line 23). Neither of these statements include any references to wider literature.

Response: The definitions of healthcare inequality and healthcare inequity used in this scoping review are widely accepted definitions in the field of health equity. These terms are used by researchers and organizations internationally, with the original definitions established in 1992 by Margaret Whitehead and the World Health Organization (see Whitehead; Int J Health Serv 1992;22:429–445).

- The term health inequity is not clearly operationalised in the review. I would expect the aims, inclusion criteria and search terms to be directed towards a list of sub-groups and possibly also towards a list of inequality types (eg stigma, bias), but I didn’t find that clearly set out. The search itself is very broad in its definition and uses a subject filter for ‘health disparities’, without any explanation of how that term relates to health inequity or health inequality. In the text the search is loosely described as covering terms ‘such as race, sexual orientation, geography etc’, which is different to the list in the Introduction (see above).

Response: We provide an accepted definition of health inequity in the first paragraph of the introduction. We also indicate (end of Step 1: Identifying the research question, p4 lines 23-25) that the focus of this scoping review is on literature examining healthcare inequalities, not health inequities. Health inequalities can be assessed via differences in measurable outcomes while the health inequities, which are a specific type of health inequality, requires a judgement of whether the differences are unfair or unjust. The search strategy was developed to reflect that focus on health inequality and not health inequity.

The National Library of Medicine Health Disparities search filter was recommended by the academic health sciences librarian who assisted in this search strategy development (as indicated in the protocol). This search filter was developed to identify studies of health inequalities and disparities as well as studies examining populations defined by equity stratifiers, such as race and sexual orientation. While we agree that the search terms are broad, this reflects the scope of the content area rather than the quality of the search strategy and is necessary to ensure that the database searches are comprehensive.

- The list of ‘research questions’ (p5) is a mix of questions and objectives. A number of topics are loosely raised, including:
-‘Measures and statistical methods’ used to evaluate end-of-life cancer care inequalities. ‘Measures’ is not defined, making it unclear whether the review will extract cancer care outcome measures or measures of inequity or measures to describe population sub-groups (eg ethnic or gender categories). Later this is expanded to include ‘study design, measures and statistical and analytical techniques’.

Response: The section “Step 1: Identifying the research question” identified the one question that we are aiming to answer with this review and expands on that research question statement by providing further details of what aspects of study methodology we will be evaluating via the scoping review. The information on what information will be extracted from the reviewed articles is detailed in Step 4, in accordance with the established framework for scoping reviews used to write this protocol.

- How the methods used in the papers ‘align with recommended approaches for studying health inequalities such as ... use of a conceptual framework; consideration of intersectionality and appropriate analytic techniques’. Although this is listed as an aim, and is highlighted in the introduction, it is not operationalised in the methods: the data extraction section does not list conceptual framework or intersectionality as

items to be extracted, and there is no list of 'recommended approaches' that the data will be compared to. 'Gaps in methodology and areas for improvement in future studies'. Identification of gaps in methodology would need a different review, of methodological literature.

Response: We have amended the selected data extraction list to include conceptual framework as requested (p6 line 8). Intersectionality was already listed as a data extraction item. However, this is not an exhaustive list of all items that will be included, and as noted our intent is to develop and pilot the data extraction tool as part of the scoping review. Experts in health equity research, including members of our research team, have published research and reviews that provide guidance on appropriate methods for studying health inequalities, which we have described in the Introduction and referenced in our protocol. Our selection of data extraction items listed in Step 4 have been guided by that literature and were chosen as they each assess an aspect of study methodology that is important to the quality of health inequality research. These data extraction items will allow us to understand what methods are commonly used in studies of health inequalities in end-of-life cancer care, which we will then interpret in the context of what methods are recommended (e.g., consideration of intersectionality and implicit biases) and what methods are not recommended (e.g., reporting only relative effects). From this review, we will be able to identify where researchers are currently doing well, with respect to designing and conducting research into health inequalities in end-of-life cancer care, and where there is room for improvement.

I feel the paper would benefit from the following amendments:

- The list of keywords could be strengthened by the addition of terms such as inequalities, protocol, scoping review.

Response: The chosen keywords are all MeSH headings. We have amended the key words list to include "Health Inequities" as suggested. While there are no MeSH headings for protocol or scoping review, if the Editor agrees that non-MeSH headings can be used as keywords, we agree that scoping review and protocol could be added as relevant keywords.

- The term 'equity stratifiers' needs to be defined at first use.

Response: We provided a definition of equity stratifier with its first use in the manuscript – see paragraph 2, line 3 of the Introduction, copied below:

"High quality health equity research requires the use of appropriate methods for investigating equity stratifiers, defined as characteristics that identify population subgroups who may experience differences in health and healthcare that may be considered unfair or unjust, such as race, ethnicity, gender, sex, religion, and socioeconomic status."

- Add the number of papers found after removal of duplicates (6p line 8).

Response: The search results were presented as preliminary to give the reader a sense of the potential size of the literature to be reviewed based on the search strategy. Given that we expected that the search strategy may change as the protocol undergoes peer review, we did not complete the process of removing duplicates nor have we finalized the number of abstracts for review.

- Add the important dates for the review, either actual or anticipated (eg start date, search date, completion of data extraction).

Response: The scoping review search dates (January 1, 2010 to December 31, 2021) were described in the Study Selection description (p5 lines 43-44). Given that we are waiting to start the review until

the protocol is accepted for publication, we have not yet identified dates for key milestones in the review process, such as the start date or completion of data extraction, as those are dependent on the peer review and journal response times. These are not standard in the reporting of scoping review protocols or systematic review protocols as per standard guidelines (e.g., Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols, Johanna Briggs Institute scoping review protocol reporting checklist).

- Inclusion of the data charting table as an appendix.

Response: We have provided a list of data charting items in the Data Extraction setting. Thus, we do not see the value of including a charting table as an appendix when all items that would be included in that table are already described in the protocol text. However, we could remove the content from the text and include as a supplementary appendix if that would be preferable.

- Mention of bias is currently included in the data extraction section: if bias is to be considered, it would be more appropriate in a separate 'Risk of bias' section of the protocol, with a description of how that will be assessed.

Response: We agree that this requires clarification. Our protocol originally stated that we would extract 'remaining sources of potential bias.' This was referring to biases that may arise through the study design, study population selection, variable measurement, confounder selection and control, and statistical analysis. We have revised the Data Extraction setting to remove 'remaining sources of potential bias' and include these specific study characteristics as data extraction items (p6 lines 11-20).

The protocol also indicated that data extraction would capture any discussions of implicit bias in the reviewed studies. These are biases that are held by researchers that may unknowingly impact how they approach, conduct, and interpret research into health inequalities. Experts in the field (e.g., Harper et al., doi: [10.1111/j.1468-0009.2010.00587.x](https://doi.org/10.1111/j.1468-0009.2010.00587.x)) recommend that researchers explicitly consider and discuss any normative judgements that may underlie their research. This data extraction item is intended to capture if the discussion of any reviewed studies included statements on implicit biases.

- Data extraction include the 'results'. Many of the studies in the review may not have health inequity as their main purpose, so the primary results might not be of interest to this review. There is a need for a clear definition of which results the review will extract.

Response: We agree that this could be clarified in a revision. We have revised the sentence as follows (see p6, line 13):

Key areas abstracted in the chart will include the healthcare system and region where the study was conducted, description of data sources, study timeframe, sample size, cancer site, description of the equity stratifier and how it was measured (individual or neighbourhood level, reference group, continuous or categorical, summary measures), description of the study outcome and how it was measured, statistical methods used to identify the relationship between the equity stratifier and outcome, effect measures used (relative or absolute), confounders controlled for, remaining sources of potential bias, and results describing relationships between equity stratifiers and end-of-life outcomes.

- Provide an explanation of why no patients or public were involved in the review, given how relevant this topic is to patients.

Response: This section is reported in accordance with BMJ Open requirements, which specify that protocols must identify if patients or the public were involved in the review, and if yes, how they were engaged. No justification is requested from authors who did not engage with patients or the public. However, we do plan to engage patients in the evidence synthesis and interpretation of this scoping review, working with a leadership panel of patients established by Dr. Mahar (senior author) as part of a research program examining health equity in cancer care. This section of the manuscript has been revised for clarification (p6 lines 36-37).

- The protocol is not written using any reporting guidelines. If there are no reporting guidelines for scoping reviews, perhaps the reporting guideline for systematic reviews could be adapted for this purpose: Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA. Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) 2015 statement. *Syst Rev.* 2015;4(1):1. doi: 10.1186/2046-4053-4-1.

Response: At the time this protocol was written, there were no reporting guidelines that were specific to scoping review protocols (PRISMA-P is specific to systematic reviews and meta-analyses, which use different methods and approaches than scoping reviews). As noted in the Methods (p4, lines 4-5), we designed the scoping review using established methods developed by Arksey and O'Malley and later expanded by Levac et al. We also note that the scoping review will be reported in accordance with relevant reporting guidelines, including the Preferred Reporting Items for Systematic reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) and PRISMA guidelines for equity-focused systematic reviews (PRISMA-E).

In April 2022, the Johanna Briggs Institute published guidance on items to report in a scoping review protocol (Peters M, Godfrey C, McInerney P et al. Best practice guidance and reporting items for the development of scoping review protocols, *JBI Evidence Synthesis: April 2022 - Volume 20 - Issue 4 - p 953-968*). We have made the following minor changes to ensure our protocol is reported in accordance with these recommendations:

- Added corresponding author mailing address to title page
- Noted that amendments will be documented and published with the scoping review results (p4 lines 11-12)
- Noted that the funders of this project had no role in the development of this protocol (p7 line 41)

- The review will include both qualitative and quantitative papers, but throughout the paper more attention is given to the quantitative papers, and there is insufficient description of how the qualitative papers will be dealt with at each stage of the review.

Response: We agree that some data extraction items are only relevant to quantitative studies (e.g., statistical methods used to identify the relationship between the equity stratifier and outcome, effect measures used, confounders controlled for). We have amended the data extraction section to specify that those extraction items specific to quantitative studies. For qualitative studies, we have added the following data extraction item: themes related to relationships between equity stratifiers and end-of-life outcomes. This is similar to our approach with a prior scoping review protocol published in the BMJ Open (Stirling M, Linton J, Ouellette-Kuntz H, et al. Scoping review protocol documenting cancer outcomes and inequalities for adults living with intellectual and/or developmental disabilities. *BMJ Open.* 2019 Nov;9(11):e032772) and published in full in the *European Journal of Oncology Nursing* (Stirling M, Anderson A, Ouellette-Kuntz H et al. A scoping review documenting cancer outcomes and inequities for adults living with intellectual and/or developmental disabilities. *European Journal of Oncology Nursing.* 2021 Oct;54:102011).

- The three broad categories of search terms are described in the Methods section as cancer, end-of-life and health inequalities. Yet, in the Medline search, 'cancer' only appears as an AND term

with 'end-of-life', so the search will have identified many end-of life studies outside of cancer, which will not be relevant for the review.

Response: The search strategy includes three broad search categories, all combined by AND: cancer AND end-of-life care AND equity stratifiers. The latter two search categories each have numerous search terms within them, joined by OR, given the various terms that can be used in database indexes (e.g., palliative care OR end-of-life OR terminal care). With cancer as a required search term, the search will only identify studies that examine end-of-life care specific to cancer patients. Studies outside of cancer should not be identified through the search, unless studies look across diagnoses, including those dying of cancer and non-cancer illnesses.

Reviewer: 2 Dr. Matthew Carey, Churchill Hospital
 Comments to the Author:

Overall this is a good summary of the protocol to be used to answer the question regarding inequalities in outcomes for end of life care in cancer patients. I look forward to reading the results in the future.

Page 4, lines 29-34 - the sentence is very long and difficult to follow, please consider splitting to make easier to read and understand.

Response: We have amended the sentence as follows (p3, lines 23-28):

Appropriate methods include the use of causal frameworks to inform the research question, theory-driven selection and measurement of equity stratifiers and covariates, and consideration of intersectionality and interactions among equity stratifiers. Further, appropriate analytic approaches should be applied, including principled approaches to covariate adjustment, considering appropriate reference groups and reporting both additive and relative effects.^{5,7,9}

VERSION 2 – REVIEW

REVIEWER	Cotterill, Sarah University of Manchester, Centre for Biostatistics
REVIEW RETURNED	06-Jun-2022

GENERAL COMMENTS	<p>Thank you for providing the revised manuscript and the point-by-point response to my previous comments.</p> <p>I want to start by apologising that I failed to read the cover letter carefully, and wrongly assumed that this review was already underway. Many of my comments were based on that assumption, and I would have not made those comments if I had understood that the review is still at the planning stage and the protocol can be further developed, both before the review starts and in the early stages.</p> <p>I should make clear that I am not a specialist in health inequalities research. However, I think it is important that the protocol terms and procedures are clear to researchers, like me, who are outside the specialist field. To that purpose, I suggest the following small changes:</p> <ul style="list-style-type: none"> • Add suitable references at the end of the sentence 'These variations in care represent health inequalities, defined as ...or groups' (p3, lines 6-8) even if these are the same references that are provided for the subsequent definition of health inequities.
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	<ul style="list-style-type: none"> • Make clear how equity stratifiers will be operationalised in the review. Currently there is one list of equity stratifiers in the Introduction (p3, lines 15-18) and a different list in the inclusion criteria (page 5, lines 31-33). In both places the authors make clear that these are only some of the stratifiers rather than a full list. It would be difficult for a reviewer to operationalise these lists as inclusion/exclusion criteria. It would be helpful to add a definitive list of equity stratifiers, but I realise that may not be possible. If it is not possible, then the authors will need to provide some other guidance in the Exposure section, in order that both the reviewers and the reader are clear how the inclusion/exclusion decision will be made. Alternatively, the Exposure section of the inclusion criteria could be amended to indicate that there will be some process developed to decide on the criteria (such as assessing a sample of studies first to gain a better understanding of the field and develop more specific criteria). My other comments have been addressed, successfully rebutted, or are not relevant now I realise the scoping review is yet to start.
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VERSION 2 – AUTHOR RESPONSE

Reviewer 1: Dr. Sarah Cotterill, University of Manchester

Thank you for providing the revised manuscript and the point-by-point response to my previous comments. I want to start by apologising that I failed to read the cover letter carefully, and wrongly assumed that this review was already underway. Many of my comments were based on that assumption, and I would have not made those comments if I had understood that the review is still at the planning stage and the protocol can be further developed, both before the review starts and in the early stages.

I should make clear that I am not a specialist in health inequalities research. However, I think it is important that the protocol terms and procedures are clear to researchers, like me, who are outside the specialist field. To that purpose, I suggest the following small changes:

1. Add suitable references at the end of the sentence ‘These variations in care represent health inequalities, defined asor groups’ (p3, lines 6-8) even if these are the same references that are provided for the subsequent definition of health inequities.

Response: We have revised the manuscript to add appropriate references at the end of this sentence. See pg. 3 line 8. Note that this revision was not highlighted via track changes.

2. Make clear how equity stratifiers will be operationalised in the review. Currently there is one list of equity stratifiers in the Introduction (p3, lines 15-18) and a different list in the inclusion criteria (page 5, lines 31-33). In both places the authors make clear that these are only some of the stratifiers rather than a full list. It would be difficult for a reviewer to operationalise these lists as inclusion/exclusion criteria. It would be helpful to add a definitive list of equity stratifiers, but I realise that may not be possible. If it is not possible, then the authors will need to provide some other guidance in the Exposure section, in order that both the reviewers and the reader are clear how the inclusion/exclusion decision will be made. Alternatively, the Exposure section of the inclusion criteria

could be amended to indicate that there will be some process developed to decide on the criteria (such as assessing a sample of studies first to gain a better understanding of the field and develop more specific criteria).

Response: We have revised the Introduction to clarify that the list of equity stratifiers are examples and not an exhaustive list of all equity stratifiers. See pg. 3 line 18.

We have also revised the Methods to clarify that we will use the PROGRESS-Plus framework to inform our definition of equity stratifiers. This framework offers a definition of equity stratifiers that has been adopted by the Cochrane and Campbell Collaborations and has been incorporated into PRISMA guidelines for equity-focused systematic reviews. See pg. 5 lines 33-40 for revised text.

3. My other comments have been addressed, successfully rebutted, or are not relevant now I realise the scoping review is yet to start.

Response: We thank the reviewer for reconsidering their previous review and taking the time to provide further feedback on our manuscript.