PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Public versus patient health preferences: Protocol for a study to elicit EQ-5D-5L health state valuations for patients who have survived a stay in intensive care
AUTHORS	Halling, Christine; Gudex, Claire; Perner, Anders; Jensen, Cathrine; Gyrd-Hansen, Dorte

VERSION 1 – REVIEW

REVIEWER	Garratt, Andrew Norwegian Institute of Public Health, Division for Health Services
REVIEW RETURNED	10-Nov-2021

GENERAL COMMENTS	This was an interesting study protocol and the results should make an important a contribution to the literature on the role of those experiencing health states in valuation tasks. If I have one major concern, then it relates to the considerable scope of the study, including the development of an alternative value set for the EQ-5D for this healthcare setting. I wonder whether authors might be better to focus more on the development of the questionnaire including further items to assess changes in preferences. Single items often have important limitations in terms of measurement properties which may pose a problem in the measurement of complex constructs, including quality of life and preferences. This is a relatively new area and I would like to see more focus on underpinning methodology and its quality rather than the construction of a value set. 1. Abstract, Introduction. Appropriateness is rather a vague word in this context. "…which may have implications for cost per quality adjusted life year comparisons". 2. Strengths and limitations, Article summary. The statement below is rather strong. The findings, as much as they are conclusive, will be based on one study with one patient group and one methodology. Moreover, there is a limited body of work with which the results might be compared. "If the study finds no differences between the ICU patients' and public preferences, a more general involvement of patient valuations in QALY calculations is unlikely to impact markedly on the conclusions drawn in economic evaluations". 3. Introduction. QALY. The statement below might be adequate for health state preference measurement more generally, but this is in the context of the EQ-5D/EQ-VT where as far as I am aware, no national value sets exist that are based on patients. That is, value sets that have been accepted for their intended purpose in priority setting. "Valuations are based on prior valuations expressed by the general

	population (or patients) using stated preference methods. In our study, these preferences will be obtained using the EQ-VT". 4. Page 7, line 59. The readership might not be familiar with EQ-VT and cTTO. I recommend use of a sentence early on along the lines of "EQ-5D-5L health state preferences will be obtained through the use of EQ-valuation technology (EQ-VT) which is based on computer assisted face-to-face interviews and use of the composite time trade-off (cTTO)" with appropriate references. 5. Page 8. Given the scope of this article, I see no reason for the paragraph relating to the standard gamble and the TTO which might confuse some readers including terminology such as "cardinal preferences". Moreover, the SG has had considerable use in the measurement of health state preferences and was chosen for the PROMIS-29 PROPr. For comparative purposes, the current study must follow the EQ-5D valuation protocol including the use of cTTO, which was used to collect Danish values/preferences. I recommend starting with EQ-VT, the overarching framework for the elicitation of patient preferences, before describing the cTTO. This, including the widespread use of EQ-VT as described, better sets the context for measurement. 6. Page 9, para 2. This is somewhat confusing with two estimates. "The interview is estimated to take approximately one hour including all steps…" Moreover, the estimate of 30-40 minutes is rather conservative. The DCE is not included, but 5 additional cTTO states will take a good deal longer than the usual DCE questions. I envisage that these interviews if well conducted, will take on average 1.25 – 1.5 hours. Some pilot work might be necessary here, simply because of the potential respondent burden. Perhaps the authors have further information available on which these estimates are based? 7. Health state blocks. What is meant by lower (decreased) inclusion rate? Completion, participation? Please be more concrete. 8. Page 9, lines 57. Please explain what blocks are. For example, "Blocks represent a randomized allocation of health states to ensure that enough health states are valued to give preference estimates that are statistically robust". 9. Page 9. Is the reduction in blocks and ensuing increase in number of health states based on EuroQol recommendations or scientific publications? Or are we are an earlier phase of development? Please state and provide references where available. 10. Page 11, line 10. Is it not more the case that quality control is discussed at appropriate intervals, dependent on the quality of the data? If so, please be more precise. 11. Comparison of patient and public valuations. The timing of the data collection should come earlier in the methods section. For example, at the end of 2.1.1. 12. Page 11, final para. I found this difficult to follow. "Comparisons of patient and general public preferences will be based on three forms of analysis"? 13. The overall interview content is summarized under Table 1 and

	in the Appendix, but it is important that further detail is provided about the number and content of questions under 3. Have these questions been used before? If so, please provide references. If they have been developed for the purpose of this study, then the methods of development should be briefly described together with any cognitive debriefing interviews to assess acceptability, comprehensibility etc. Moreover, are there plans to pilot these questions? What is meant with “importance of quality of life” (page 12, line 49)? These questions should all be fully described earlier under the content of the questionnaire so that the analysis section can be made more concise and clearer. 14. To adequately capture any changes in the quality/quantity trade-off is always going to prove very difficult given that 1-3 years are involved. One question might prove inadequate. I am unsure as to whether all respondents will understand the link between this question and the cTTO tasks they have just completed. Are items and/or scales available which assess this construct? I understand that this might make for a difficult literature search, for example, within the field of psychology. I would at least recommend some open-ended questions to get the patient to think about whether or how they considered these issues pre-ICU. There is a danger of interviewer-bias with such approaches, but recommendations exist. “Compared to now, how did you think about the duration of your life before the hospital stay 1-3 yrs ago?...“Compared to now…your health including mobility…angst/depression compared to before the hospital stay”. These questions could also be closed with response choices. Having several questions will certainly give a better indication of changes in preferences if indeed they are measurable. 15. 2.3 Investigating the heterogeneity in preferences. Given the lag of 1-3 yrs before the cTTO interview, might recall bias be a problem when asking patients about whether their preferences have changed? Operationalising such concepts in terms of questions poses serious challenges. Recall bias will only serve to enhance problems with reliability and validity. 16. This brings me to another important problem, patient preferences for health might well have changed through the natural ageing process, and particularly for those of certain ages (45 years and over?). This might well contaminate the analysis for people who are now 1-3 yrs older. 17. 2.3 continued. This section is concerned with analysis. However, the interview content is expanded upon when this would not be required had it been adequately covered earlier in the methods. 18. Line 49. Given the important impact of the ICU stay on health, there might be very few patients who have a prior experience of illness to rival this. 19. Page 12, line 60. Given that there have been few attempts to compare patient and public preferences, what purpose might such a value set serve? Is not the remainder of this paragraph testable by means of multivariable analyses? Or is the value set more an accepted method of presentation which can further help highlight any differences?

	20. Page 13, 3. Recall bias is of further concern in the analyses relating to health state reference dependency. Can we reliably and validly assess pre-ICU preferences based on recall of 1-3 years ago? 21. 2.5 Discussion, Page 14, line 36. Spikes, gaps and clusters should be explained. Given the nature of this research, might stronger QC procedures be warranted as a means of tracking and dealing with such issues? 22. Page 15, para 2. It is reasonable to argue that the ICU experience will more than outweigh any impact of C-19 on preferences. 23. Terminology could both be simplified and more consistent. For example, rather than cTTO or TTO, I would prefer the use of ”EQ-5D valuation” as found in the Abstract and particularly where the interviews are mentioned more generally. For example, page 15, line 37. I understand that some economists have their own preferences here, but this is not a health economics journal. This survey is based on EQ-VT, and hence might it not be best to stick with values and valuation rather than preferences? Minor Abstract, Methods. “and EQ-5D dimensions, where the patient…” “Serious health events” rather than “shock”? Page 9. “health state” rather than “frailty”. Table 1. Delete “so-called”. The quality control process is not part of the interview. Please remove. Page 9, line 30 “…discrete choice tasks to minimize respondent burden.”. Page9, lines 33-34 “…if undertaken with an average member…” Page 9, line 60. “…is being used to elicit..” Page 10, line 8. “Previous studies have used approximately…” Page 11, line 6-7. “…QC process has been shown to improve interviewer protocol compliance and data quality” Page 12, line 43. Use “assess” rather than “verify”. Page 14, line 47. Replace “eliciting technics” with “elicitation methods”.

REVIEWER	Vietri, Jeffrey Pfizer Inc, Value & Evidence Employment and shareholder of Pfizer, Inc.
REVIEW RETURNED	15-Dec-2021

GENERAL COMMENTS	This protocol describes a promising study which aims to generate preferences for EQ-5D-5L health states among survivors of intensive care unit stays, compare these valuations to the recent standard value set for Denmark, and explore associations between ICU survivors’ valuations and their demographic and disease characteristics. I believe it is worthy of publication but I have a few suggestions for minor improvements. One suggestion is to revise the title of the manuscript to reflect that the participants in the study are ICU survivors, not current ICU patients. “Patients in intensive care” generally means patients who are currently in intensive care, not those with recent experience of intensive care.

	On page 4, I suggest rephrasing to indicate the five levels range from no problems to extreme problems, as “severe” is the 4th of the 5 levels of impairment of the English language EQ-5D-5L, with the 5th being “…extreme problems” or “…unable to” depending on the domain. Health state reference dependency is presented in quotes on page 7 as part of one of the research questions, but the term does not appear in the introduction prior. It should be named and discussed in the introduction rather than introduced later. Although the inclusion criteria are mention, I did not see details on exclusion criteria. I found myself wondering how ICU stays subsequent to those associated with the trials mentioned would be incorporated in the analysis, or if they would disqualify patients from participating in the current study. I suggest explicitly addressing these criteria (i.e., either listing the criteria or stating that there are none). In section 2.2, the term, “pre-differences” is used, which I found confusing. Perhaps there is a better term or phrase? I assume this is describing the differences in personal characteristics between the general population and ICU-experienced sample aside from the ICU stay. In section 3 there is a statement that ethics approval is not needed for the valuation study, but why? In some places such a study would probably require approval from an ethics committee or institutional review board, so some explanation should be given (for instance, if national regulations exempt such studies from oversight).

VERSION 1 – AUTHOR RESPONSE

Reviewer #1:	**Reply**
This was an interesting study protocol and the results should make an important a contribution to the literature on the role of those experiencing health states in valuation tasks.	Thank you.
If I have one major concern, then it relates to the considerable scope of the study, including the development of an alternative value set for the EQ-5D for this healthcare setting. I wonder whether authors might be better to focus more on the development of the questionnaire including further items to assess changes in preferences. Single items often have important limitations in terms of measurement properties which may pose a problem in the measurement of complex constructs, including quality of life and preferences. This is a relatively new area and I would like to see more focus on underpinning methodology and its quality rather than the construction of a value set.	Thank you for these considerations. We have changed the references to ‘value set’ to ‘health state valuation’ to make it clearer that the study is a methodological investigation rather than generation of a value set. The generated value set will have larger standard deviations due to fewer respondent than in other valuation studies (300 vs. 1,000 respondents). ‘Value set’ does have wider implications of being definitive and widely tested in terms of differences between health states, larger sample size, etc. We have added the following in the discussion section: “This study is primarily a methodological investigation. We will be generating a value set to answer methodological questions. The establishment of a patient value set that can be used for prioritisations will require a larger sample size in order to produce more robust valuation estimates.”

1. Abstract, Introduction. Appropriateness is rather a vague word in this context. "…which may have implications for cost per quality adjusted life year comparisons".	Thank you for this comment. We have changed accordingly.
2. Strengths and limitations, Article summary. The statement below is rather strong. The findings, as much as they are conclusive, will be based on one study with one patient group and one methodology. Moreover, there is a limited body of work with which the results might be compared. "If the study finds no differences between the ICU patients' and public preferences, a more general involvement of patient valuations in QALY calculations is unlikely to impact markedly on the conclusions drawn in economic evaluations".	Thank you for this comment. This bullet point is now removed (also due to editor's comment)
3. Introduction. QALY. The statement below might be adequate for health state preference measurement more generally, but this is in the context of the EQ-5D/EQ-VT where as far as I am aware, no national value sets exist that are based on patients. That is, value sets that have been accepted for their intended purpose in priority setting. "Valuations are based on prior valuations expressed by the general population (or patients) using stated preference methods. In our study, these preferences will be obtained using the EQ-VT".	Thank you for this comment. We have changed the paragraph to the following: "The EQ-5D-5L has five levels within each dimension, ranging from no problems to extreme problems, for example from "no problems walking" to "unable to walk".(4) To translate these health states into QALY weights, each health state is valued on a scale, where 0 is equivalent to being dead and 1 indicates full or perfect health. The specific value assigned to each health state is based on valuations expressed by respondents using stated preference methods."
4. Page 7, line 59. The readership might not be familiar with EQ-VT and cTTO. I recommend use of a sentence early on along the lines of "EQ-5D-5L health state preferences will be obtained through the use of EQ-valuation technology (EQ-VT) which is based on computer assisted face-to-face interviews and use of the composite time trade-off (cTTO)" with appropriate references.	Thank you for this comment. We have added the following sentence to the beginning of the Methods and analysis section: "EQ-5D-5L health state preferences will be obtained using the EQ-valuation technology (EQ-VT) which is based on computer assisted face-to-face interviews and use of the composite time trade-off (cTTO) (25,26), see section 2.1.2 for more details."
5. Page 8. Given the scope of this article, I see no reason for the paragraph relating to the standard gamble and the TTO which might confuse some readers including terminology such as "cardinal preferences". Moreover, the SG has had considerable use in the measurement of health state preferences and was chosen for the PROMIS-29 PROPr. For comparative purposes, the current study must follow the EQ-5D valuation protocol including the use of cTTO, which was used to collect Danish values/preferences. I recommend starting with EQ-VT, the overarching framework for the elicitation of patient preferences, before describing the cTTO. This, including the widespread use of EQ-VT as described, better sets the context for measurement.	Thank you for this comment. We agree and have changed accordingly.
6. Page 9, para 2. This is somewhat confusing with two estimates. "The interview is estimated to take approximately one hour including all steps…" Moreover, the estimate of 30-40 minutes is rather	Thank you for your input on this matter. We have conducted some pilot interviews which on average took one hour. But we agree that in this setting with previous ICU patient (where

conservative. The DCE is not included, but 5 additional cTTO states will take a good deal longer than the usual DCE questions. I envisage that these interviews if well conducted, will take on average 1.25 – 1.5 hours. Some pilot work might be necessary here, simply because of the potential respondent burden. Perhaps the authors have further information available on which these estimates are based?	some are expected to be quite ill still), we might need to presume more than one hour. We have changed the section to only have one estimate on 1.5 hours.
7. Health state blocks. What is meant by lower (decreased) inclusion rate? Completion, participation? Please be more concrete.	Thank you for pointing this out. We have changed accordingly.
8. Page 9, lines 57. Please explain what blocks are. For example, “Blocks represent a randomized allocation of health states to ensure that enough health states are valued to give preference estimates that are statistically robust”.	Thank you. We have changed accordingly.
9. Page 9. Is the reduction in blocks and ensuing increase in number of health states based on EuroQol recommendations or scientific publications? Or are we are an earlier phase of development? Please state and provide references where available.	Both. So this is added: “This approach is recommended by EuroQol and is being used to elicit the (not yet published) Australian EQ-5D-5L value set.(40)” Thank you.
10. Page 11, line 10. Is it not more the case that quality control is discussed at appropriate intervals, dependent on the quality of the data? If so, please be more precise.	Thank you. We have changed accordingly.
11. Comparison of patient and public valuations. The timing of the data collection should come earlier in the methods section. For example, at the end of 2.1.1.	We agree and have moved the section accordingly.
12. Page 11, final para. I found this difficult to follow. “Comparisons of patient and general public preferences will be based on three forms of analysis”?	We have changed accordingly.
13. The overall interview content is summarized under Table 1 and in the Appendix, but it is important that further detail is provided about the number and content of questions under 3. Have these questions been used before? If so, please provide references. If they have been developed for the purpose of this study, then the methods of development should be briefly described together with any cognitive debriefing interviews to assess acceptability, comprehensibility etc. Moreover, are there plans to pilot these questions? What is meant with “importance of quality of life” (page 12, line 49)? These questions should all be fully described earlier under the content of the questionnaire so that the analysis section can be made more concise and clearer.	Thank you for this comment. We have added the following: “Most of the background and contextual questions were used in the Danish EQ-5D-5L valuation study with the Danish general population, thus enabling comparisons between the patient and general population settings. The first three and last ten questions in Appendix A have been developed for the current study to help interpret patients’ responses and investigate heterogeneity in cTTO responses. These questions were tested in a pilot study with 10 persons. To avoid influencing the cTTO valuation, the questions are placed at the end of the interview. Two questions explore potential changes in the patient’s reluctance to trade off longevity for HRQoL: “Would you have answered differently before the ICU stay? Would you have been willing to ‘sacrifice’ more/fewer years for quality of life before the ICU stay?” The last ten questions ask background information including age, number of children, reason for

	ICU admission, and recovery time after ICU stay." The "importance of quality of life" has been replaced by "the relative importance of the EQ-5D dimensions for quality of life".
14. To adequately capture any changes in the quality/quantity trade-off is always going to prove very difficult given that 1-3 years are involved. One question might prove inadequate. I am unsure as to whether all respondents will understand the link between this question and the cTTO tasks they have just completed. Are items and/or scales available which assess this construct? I understand that this might make for a difficult literature search, for example, within the field of psychology. I would at least recommend some open-ended questions to get the patient to think about whether or how they considered these issues pre-ICU. There is a danger of interviewer-bias with such approaches, but recommendations exist. "Compared to now, how did you think about the duration of your life before the hospital stay 1-3 yrs ago?..."Compared to now…your health including mobility…angst/depression compared to before the hospital stay". These questions could also be closed with response choices. Having several questions will certainly give a better indication of changes in preferences if indeed they are measurable.	Thank you for these considerations. See previous reply about the explanation of included questions. We have now explained the question (Would you have been willing to "sacrifice" more/less years for quality of life before the ICU stay?) in the manuscript. The questions have been piloted on 10 persons, who all understood the issue about the quality/quantity trade-off. To make it even clearer, we have added this to the question: "Think about the questions where you had to choose between life A and life B."
15. 2.3 Investigating the heterogeneity in preferences. Given the lag of 1-3 yrs before the cTTO interview, might recall bias be a problem when asking patients about whether their preferences have changed? Operationalising such concepts in terms of questions poses serious challenges. Recall bias will only serve to enhance problems with reliability and validity.	Thank you for this important input. Recall bias is a concern. We have added the following in the discussion: "Given the lag of 1-3 years from the ICU stay to the valuation interview, recall bias may impact on responses when we ask patients about whether their preferences have changed. Recall bias is particularly an issue when we pose questions such as 'Would you have answered differently before the ICU stay? Would you have been willing to 'sacrifice' more/fewer years for quality of life before the ICU stay?' These questions will be used to support a discussion of possible explanations for differences in valuations. We will seek to provide evidence on a potential presence of recall bias by comparing responses provided with a lag of 3 years versus responses provided after only 1 year. "
16. This brings me to another important problem, patient preferences for health might well have changed through the natural ageing process, and particularly for those of certain ages (45 years and over?). This might well contaminate the analysis for people who are now 1-3 yrs older.	Thank you for this comment. We compare the patients' preferences with those of the general population and adjust for age differences, see section 2.2 'Comparison of patient and public valuations'.
17. 2.3 continued. This section is concerned with analysis. However, the interview content is expanded upon when this would not be required had it been adequately covered earlier in the methods.	Thank you for this comment. We have added a section earlier in the manuscript, see answer to comment 13.

18. Line 49. Given the important impact of the ICU stay on health, there might be very few patients who have a prior experience of illness to rival this.	Yes, that is true. However, we find it important to know whether their ICU stay is for example part of a long cancer/heart/lung disease course.
19. Page 12, line 60. Given that there have been few attempts to compare patient and public preferences, what purpose might such a value set serve? Is not the remainder of this paragraph testable by means of multivariable analyses? Or is the value set more an accepted method of presentation which can further help highlight any differences?	Thank you for these important considerations. We estimate the value set to have metrological discussions on differences in preferences between the patients and those of the general population. We have deleted the last part of the paragraph and have inserted the following: “The question is: Would you have been willing to ‘sacrifice’ more/fewer years for improvements in quality of life before the ICU stay?. This item can be used to qualitative examine the patient’s own view of their willingness to trade off length of life and quality of life. This question can moreover be used to examine whether the 86 directly valued health states changes according to the respondents answers. Those who respond that they are less/more willing to give up life-years after their ICU stay is expected to express higher/lower valuations for the particular health states. Further, we can assess the trade-off between longevity and HRQoL by examining all extrapolated health states by investigating the ranking of health states based on the patient’s respondents and the ranking based on the public’s respondents. If ranking of health states remain intact despite valuations being different, this would suggest that it is the value of life-years that has changed and not the preferences for specific health outcomes.”
20. Page 13, 3. Recall bias is of further concern in the analyses relating to health state reference dependency. Can we reliably and validly assess pre-ICU preferences based on recall of 1-3 years ago?	Thank you for this comment. We have added a text which addresses our concern for recall bias, see response to prior comments.
21. 2.5 Discussion, Page 14, line 36. Spikes, gaps and clusters should be explained. Given the nature of this research, might stronger QC procedures be warranted as a means of tracking and dealing with such issues?	Thank you for this comment. We have changed accordingly.
22. Page 15, para 2. It is reasonable to argue that the ICU experience will more than outweigh any impact of C-19 on preferences.	Thank you for this input. We have changed accordingly.
23. Terminology could both be simplified and more consistent. For example, rather than cTTO or TTO, I would prefer the use of ”EQ-5D valuation” as found in the Abstract and particularly where the interviews are mentioned more generally. For example, page 15, line 37. I understand that some economists have their own preferences here, but this is not a health economics journal. This survey is based on EQ-VT, and hence might it not be best to stick with values and valuation rather than preferences?	Thank you for this comment. We have changed accordingly towards more use of the terms EQ-5D valuation, values and valuation rather than preferences, TTO and cTTO.

Minor Abstract, Methods. “and EQ-5D dimensions, where the patient…” “Serious health events” rather than “shock”? Page 9. “health state” rather than “frailty”. Table 1. Delete “so-called”. The quality control process is not part of the interview. Please remove. Page 9, line 30 “…discrete choice tasks to minimize respondent burden.”. Page9, lines 33-34 “…if undertaken with an average member…” Page 9, line 60. “…is being used to elicit..” Page 10, line 8. “Previous studies have used approximately…” Page 11, line 6-7. “…QC process has been shown to improve interviewer protocol compliance and data quality” Page 12, line 43. Use “assess” rather than “verify”. Page 14, line 47. Replace “eliciting technics” with “elicitation methods”.	Thank you for these comments. We have changed accordingly.

Reviewer #2: Dr. Jeffrey Vietri, Kantar Health Inc	**Reply**
This protocol describes a promising study which aims to generate preferences for EQ-5D-5L health states among survivors of intensive care unit stays, compare these valuations to the recent standard value set for Denmark, and explore associations between ICU survivors’ valuations and their demographic and disease characteristics. I believe it is worthy of publication but I have a few suggestions for minor improvements.	Thank you.
One suggestion is to revise the title of the manuscript to reflect that the participants in the study are ICU survivors, not current ICU patients. “Patients in intensive care” generally means patients who are currently in intensive care, not those with recent experience of intensive care.	Thank you for this spot on comment. We have changed accordingly.
On page 4, I suggest rephrasing to indicate the five levels range from no problems to extreme problems, as “severe” is the 4th of the 5 levels of impairment of the English language EQ-5D-5L, with the 5th being “…extreme problems” or “…unable to” depending on the domain.	Thank you for pointing this out. We have changed accordingly.
Health state reference dependency is presented in quotes on page 7 as part of one of the research questions, but the term does not appear in the introduction prior. It should be named and discussed in the introduction rather than introduced later.	Thank you for this comment. We have added this to the introduction: “Another possible reason for potential differences in preferences is if views of health states are dependent on the respondents’ own health. This is often referred to as ‘health state reference dependency’.(5)”
Although the inclusion criteria are mention, I did not see details on exclusion criteria. I found myself wondering how ICU stays subsequent to those associated with the trials mentioned would be incorporated in the analysis, or if they would disqualify patients from participating in the current study. I suggest explicitly addressing these criteria (i.e., either listing the criteria or stating that there are none).	Thank you for bringing this up. We will include patients even though they subsequently have a new ICU stay – so that is not an exclusion criteria. To be more clear about the exclusion criteria we have included the following in the section on case population and sampling:

	"In HOT-ICU exclusion criteria are for example pregnancy, chronic mechanical ventilation, and brain death. Further exclusion criteria are found in the HOT-ICU protocol.(26)" "In CLASSIC patients are excluded if they for example have septic shock for more than 12 hours at the time of screening, life-threatening bleeding, acute burn injury of more than 10% of the body surface area, and pregnancy. More information on exclusion criteria in the CLASSIC trial are found in the CLASSIC protocol.(28) The only exclusion criteria other than those from the RCTs are patient with impaired cognitive function, see section 2.1.7 for further details."
In section 2.2, the term, "pre-differences" is used, which I found confusing. Perhaps there is a better term or phrase? I assume this is describing the differences in personal characteristics between the general population and ICU-experienced sample aside from the ICU stay.	Thank you for this comment. We have changed the word to "differences in personal characteristics between the general population and the ICU patients aside from the ICU stay"
In section 3 there is a statement that ethics approval is not needed for the valuation study, but why? In some places such a study would probably require approval from an ethics committee or institutional review board, so some explanation should be given (for instance, if national regulations exempt such studies from oversight).	We have added the following: "Under Danish regulations, ethical approval is not usually required for studies of this type, and this has been confirmed by the Institutional Review Board."

VERSION 2 – REVIEW

REVIEWER	Vietri, Jeffrey Pfizer Inc, Value & Evidence Employee and stockholder of Pfizer Inc.
REVIEW RETURNED	24-Mar-2022

GENERAL COMMENTS	My concerns with the previous version of the manuscript have been adequately addressed.