PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Incorporating parent, former patient, and clinician perspectives in the design of a national UK double-cluster, randomised controlled trial addressing uncertainties in preterm nutrition
AUTHORS	Lammons, William Moss, Becky Battersby, Cheryl Cornelius, Victoria Babalis, Daphne Modi, Neena

VERSION 1 – REVIEW

REVIEWER	Reviewer name: Dr. Jos Latour Institution and Country: University of Plymouth, School of Nursing and Midwifery, Faculty of Health and Human Sciences Competing interests:None
REVIEW RETURNED	04-May-2021

GENERAL COMMENTS	bmjpo-2021-001112: Incorporating parent, former patient, and clinician perspectives in the design of a national UK double-cluster, randomised controlled trial addressing uncertainties in preterm nutrition Thank you for inviting me to review this manuscript presenting a Patient and Public Involvement (PPI) consultation. The manuscript is well written and I like to applaud the authors in starting the planned COLLABORATE trial with an important PPI consultation exercise. 1. Introduction: I main suggestion. add a paragraph about PPI that can be linked to your project/consultation aim. You have a very brief PPI section in the methods which should stay their. Suggest to use references such as the NIHR – INVOLVE national guidelines that are important to share among other paediatric researchers. Examples to look at PPI introductions: Fiori M, Endacott R, Latour JM. Public involvement in designing a study on patient-witnessed cardiopulmonary resuscitation in hospital. Nurs Crit Care. 2020;25(5):313-320. doi: 10.1111/nicc.12429.; Manning JC, Hemingway P, Redsell SA. Survived so what? Identifying priorities for research with children and families post-paediatric intensive care unit. Nurs Crit Care. 2018 Mar;23(2):68-74. doi: 10.1111/nicc.12298. 2. Methods (first paragraph): please explain the number of PPI advisers that have been recruited. This is unclear. You did 6 focus and semi structured interviews with how many ex-patients and parents? Is the 6 focus groups correct as you had 9 volunteers (as described in Results). Thus were most 'focus groups' with only 1 volunteer (which should be an interview and not a FG? Please revisit this and add the number of volunteers in this section. Also, how many FG did you do with clinicians? (There were 11 volunteers of clinicians; all in 1 FG?). 3. Methods (second paragraph): please provide detail of the qualitative analysis strategy. This is unclear. In the abstract it is stated Thematic Analysis (TA) but in the methods section it is not

	mentioned. Depending what TA strategy you opted to do, you need to described the steps of the qualitative data analysis. Perhaps visit some of the most used TA papers by Braun and Clarke: Braun V, Clarke V. Successful Qualitative Research, a Practical Guide for Beginners. London, UK: Sage Publications Ltd; 2013; Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3:77-101. 4. Methods: although PPI consultations do not need ethical approval (your participants are volunteers and not study participants), I can I suggest to add this in the methods section and refer to the NIHR-INVOLVE guidance. Some researcher/readers might be sensitive about this. Also, I see at the end of the manuscript that the volunteers were approached via the neoWONDER project with a REC number. However, the PIS is about a study on linking existing data to evaluate long-term health and wellbeing of preterm babies. Perhaps this needs to be changed to reflect the issue that a PPI consultation is not a study and thus no ethical approval is needed according to the UK national guidance. 5. Results: Table 1 might need some explanation. What does 'position attributing knowledge' and support for trial' means. What, why and how what this data collected? 6. Results: Page 7 lines 12-13: Suggest to describe in the text the named themes that belong to parents/patients and clinician and the one that is combined. 7. Results: the description/presentation of the themes. The quotations used in the text need to have a reference to the participants between brackets so this can be linked to the Table. 8. Results: quotations; I noticed that most quotations in the text are coming back in the Table too. This questions the richness and in-depth of the focus groups / interviews. Are you using only 11 quotations (Table 1) to define the themes? Possibly you need to revisit the qual data and see if you have more in-depth narratives. Although this is not a qualitative study, your volunteers deserve that you handle their data with respect and use it according to the qualitative research methods (as you are using the COREQ guidelines). 9. Discussion: first sentence 'Out study". See my comment nr 4… this was not a study, this was a PPI consultation. If you call it a study, we need to see the ethical approval (at least from the University). Suggest to start with; This PPI consultation with…. Also; revisit the full manuscript regarding this issue; including the Acknowledgments as you called there a 'pre-study' which is not the case… it remains a PPI consultation that you report here. And wording like page 12 line 12: 'Our research has identified…". Again, I think you are not reporting a research project here. 10. Discussion: Good to see the sections related to the changes you made in the proposed trial. However, the discussion might benefit from some PPI references performed in the same or other field to highlight the importance (and benefits) of PPI consultation at the early stages.

REVIEWER	Reviewer name: Ms. Mandy Daly Institution and Country: Irish Neonatal Health Alliance, Director of Advocacy and Policymaking Competing interests: None
REVIEW RETURNED	15-Apr-2021

GENERAL COMMENTS	Congratulations to the authors for addressing this very important topic and for recognising and leveraging the multi-factorial processes taking place in the Neonatal Unit for both the families and the healthcare providers in the study design. The themes explored in the patient focus groups shine a light on the unique and oftentimes individualised family NICU experience which can directly impact the success or otherwise of study recruitment. I would have a preference for input from more nursing and speech

	and language healthcare professionals in the clinician focus groups to gather input from ALL professionals involved in providing nutrition support in the Neonatal Unit in addition to a more evenly distributed gender balance. That said, the outputs from both groups are significant and when incorporated into the design of COLLBORATE and other comparative-effectiveness studies will serve to improve the experience for study participants and researchers and firmly embed the culture of collaborative research into the future.

REVIEWER	Reviewer name: Dr. Eric Vermeulen Institution and Country: VSOP Dutch patient association for rare and genetic diseases. Soest, The Netherlands. Competing interests: None
REVIEW RETURNED	11-Apr-2021

GENERAL COMMENTS	Dear authors, Thank you for the opportunity to review your work. I have indicated 'minor revisions' but my response is rather extensive, I consider my response a merely suggestions for possible improvement. I hope you can publish and finish the project successfully. I have read your paper with interest. This kind of publications is important to show how research can benefit from consultations beforehand or involvement during the study. Maybe the authors could refer to this innovative aspect in their introduction. It is very important to build knowledge about patient involvement in research and publish examples and effects. The involvement of (adult) patients has been shown to prevent research waste and to improve inclusion/retention rates and therefore to prevent failed clinical trials.[1] Involvement reduces costs.[1] The need to involve children/parents in research design, the preparation of patients' documentation and information materials to improve research protocols and enhance research participation is widely acknowledged.[2] The failure of almost 1 in 5 pediatric trials, mainly due to recruitment problems, as referred to by Shakhnovich et al. [Pica et al. (2016)][3], might have been at least partly prevented by engaging/involving parents and children in the design stage. Early involvement of patients in the trial design may result in identification of trial aspects that are less acceptable or unclear for potential participants. Adaptation of these aspects may enhance the willingness to participate in the trial.[4] There is evidence that recruitment increases with patient engagement, and that patient engagement enhances the quality of research, e.g. by the choice of relevant outcome measures.[1] Patient involvement should be seen as an integral part of designing a study.[5] The success of COLLABORATE is important because nutrition is one of the very basic treatments in neonatal care and it is time that uncertainties are resolved! For me, it is not clear whether this effort to consult parents and clinicians about the study design and study materials was part of COLLABORATE from the beginning. You mention this under 'Patient and Public Involvement'; 'At this preliminary stage of the development of COLLABORATE', so I guess it is part of total design? As a former nurse on a NICU I always regret that no nurses were involved in the clinical participants group, but it is what it is. I see that 'Patient 1' is also Paediatric nurse. So there is a chance that experiences of nurses are involved. I know that for successful trial execution on the ward a study-team that also includes nursing representation is important. I wonder what is done with the 'no' (table 1) and the 'unsure' of support for this trial. Why did they have these opinions and what is

	done to overcome this? I do not really understand the quote about theme 1, the consent process. Maybe because I am not a native speaker… 'families don't go there' and 'forget to fill out'. That refers to informed consent I presume? That families do not give consent because they forget? I consider the consent procedure an important element of this study and see only one quote mentioned in the table/text. It is good that you could adapt the written information to parent responses, having a short and longer information form is very important. I wonder if you also constructed a script for the verbal message to parents. It is clear that neonatologists have doubts about the implementation of the study and this help for the conversation might help. It is known from research that the conversation is important for parents and that clinicians often fail to tell important elements in the conversation. [6, 7] I wonder if you have also established a 'Patient Advisory Board' or something like that to ensure involvement throughout the project. The quotes under theme 3 seem to say that this is possible and helpful 'this is what we are trying to do together' and 'to approach parents in really collaborative way'. The abstract section with results mention that there is a desire for research to be a partnership between clinicians, parents, researchers. I would appreciate more information in the discussion whether this has succeeded and which effects this has for the COLLABORATE study. I very much agree with opt out in this context but for me, one reason for opt out given in the discussion 'an ongoing consent process', begs more explanation. Of course, 'opt-in' can also be organised as an ongoing process if you ask participants regularly if they still consent? I guess that no specific outcome-measures were added to the study on the basis of this consultation but it is possible that this is done after such a consultation. Same for the design of the study. That has not been adapted on the basis of this consultation. For me, a message in the 'Key messages' under 'What is known' would also be that involvement increases recruitment rates. I am unsure about the first point under 'What this study adds': 'CER can help'. I do not know if patient involvement is standard in CER. If it is, then it 'CER helps'. If it is not, you can add an item: CER should also involve parents/patients. The last point under 'What this study adds': 'understand and address their biases that inhibit trial participation'. It has potential to do this but has it also had an effect for COLLABORATE? I hope so, that would make the chances of the project to be successful larger. 1. Levitan, B., et al., Assessing the Financial Value of Patient Engagement: A Quantitative Approach from CTTI's Patient Groups and Clinical Trials Project. Ther Innov Regul Sci, 2018. 52(2): p. 220-229. 2. Luff, D., et al., Parent and Teen Engagement in Pediatric Health Services Research Training. Acad Pediatr, 2016. 16(5): p. 496-498. 3. Pica, N. and F. Bourgeois, Discontinuation and Nonpublication of Randomized Clinical Trials Conducted in Children. Pediatrics, 2016. 138(3). 4. Crocker, J.C., et al., Impact of patient and public involvement on enrolment and retention in clinical trials: systematic review and meta-analysis. BMJ, 2018. 363: p. k4738. 5. Edelman, N. and D. Barron, Evaluation of public involvement in research: time for a major re-think? J Health Serv Res Policy, 2016. 21(3): p. 209-11. 6. Lentz, J., et al., Paving the way to a more effective informed consent process: Recommendations from the Clinical Trials Transformation Initiative. Contemp Clin Trials, 2016. 49: p. 65-9.

	7. Koyfman, S.A., et al., Informed consent conversations and documents: A quantitative comparison. Cancer, 2016. 122(3): p. 464-9.

VERSION 1 – AUTHOR RESPONSE

Manuscript ID bmjpo-2021-001112 entitled "Incorporating parent, former patient, and clinician perspectives in the design of a national UK double-cluster, randomised controlled trial addressing uncertainties in preterm nutrition"
Word count: 2977/2500
Abstract: 258/300

Editorial comments
Delete Table 2 and expand the quotes in the text. The quotes are easier to comprehend within the text

Response:
We have removed Table 2 from the manuscript, and added the quotes to the text. Please note that this has resulted in us exceeding the journal's requested word limit.

We have added the following to the results section: (Page 8, Line 25)
"…my mum will share with me that she cried with her breasts bleeding, trying to express because she was told it was the best... And she had a woman sitting next to her in the expressing room who had, you know, 500 mils of milk sitting there…and this woman was saying, 'Oh, it's not enough.' My mum was like, 'you're kidding me. I've got five ml from the last four hours. And I'm bleeding into it.'
(Page 8, Line 33)
"I remember when they talked about putting him onto formula, I said to the consultant, 'I'm really, really worried about him getting NEC [necrotising enterocolitis]. I'm really worried.' Cause I had it and…I know how bad it is…they assured me that the risk with formula was just as high as it was with donor milk. So I was like…if they need to gain weight and it's such a balancing act, isn't it?...I suppose it's the same for the doctors. They're just trying to balance the best options."
(Page 8, Line 40)
"… And at the end of the day, it has to be what's best…for your circumstances and what's best for your baby because your mum's milk is best, but if mum's milk is not available… you shouldn't make mums feel as if they're kind of a failure."
(Page 8, Line 48)
"…I appreciate the opt-out allows a much larger number of people, and often families don't go there. Not because they don't necessarily want to do it, but for whatever reason they have…they're not thinking about it or they read [the consent form]…and forget to fill out..."
(Page 9, Line 16)
"They need to be able to sometimes slightly dumb it down so we can understand it really well… I'm focusing on 'add extra protein and carbohydrate' [in the parent information leaflet.] I've never heard of that before…"
(Page 9, Line 36)
"I think this whole thing about us having to approach parents in a really collaborative way around the importance of…feeding…managing their expectations and their understanding of what is happening with that baby's gut, and that we're trying to help promote a healthy gut, not just for the time when they're in their unit, but beyond that time as a healthy gut for life – here is the one of the fundamental things that's going to influence their feeding for not just weeks, but months and years to come."
(Page 9, Line 51)
"…I had this baby ripped from me…I didn't see her after birth. It was horrific…her first nappy was changed by somebody else... All her cares were done by somebody else. The first person she saw was somebody else…"
(Page 10, Line 13)
"I'm the sort of person that likes to know everything, so I would want to read every tiny little detail of everything…but I know from speaking to other parents in the neonatal unit that a lot of parents…don't want to be involved as much and they don't want to know things."
(Page 10, Line 27)
"On a ward round, one negative sentence, a loose comment about something … just spoils everything.

We try to police that to some extent [and] share all our anxieties and disagreement beforehand ….we have our own personal agendas or personal biases but keep them to ourselves when we are … in front of other people. that's where I see the issue about [a] unit that's sort of consenting to participate, but not then sticking to the protocol…and then bringing some of their own ideas into the consenting … [and] recruitment process"
Reviewer comments
We are grateful to the referees for their suggestions.

REVIEWER COMMENTS:
Reviewer #1
1.1 Reviewer comment: I have read your paper with interest. This kind of publications is important to show how research can benefit from consultations beforehand or involvement during the study. Maybe the authors could refer to this innovative aspect in their introduction. It is very important to build knowledge about patient involvement in research and publish examples and effects.

Response: We have added the following to the introduction to illustrate this at an earlier point in the paper: (Page 5, Line 29)
These clinical uncertainties, which affect the care provided to babies as well as the information provided to families, present an opportunity to understand how parents of very preterm babies can improve the recruitment materials for the COLLABORATE trial and clarify the acceptability of consent methods, as well as compare their views and reactions with those of clinicians. PPI consultations are enriching mechanisms to improve design, making studies more successful and relevant to their stakeholders. [8-12] In paediatric research they have identified important guiding themes for future research, largely through centring the narratives and experiences of survivors and families. [13-14]
Fiori, M., Endacott, R., & Latour, J. M. Public involvement in designing a study on patient-witnessed cardiopulmonary resuscitation in hospital. Nursing in Critical Care, 2020;25:313–320. https://doi.org/10.1111/nicc.12429;
INVOLVE, NIHR. Patient and public involvement in research and research ethics committee review. NIHR. Version 1. 2009. https://www.invo.org.uk/wp-content/uploads/2011/12/INVOLVENRESfinalStatement310309.pdf. Accessed 5/2021.
INVOLVE, NIHR (National Institute of Health Research). Public involvement in research: impact on ethical aspects of research. 2014. www.involve.nihr.ac.uk. Accessed 05/2021.
Bliss: For babies born premature or sick. Our approach to research. https://www.bliss.org.uk/research-campaigns/research. Accessed 05/2021.
National Institute for Health Research. Patient and public involvement in health and social care research: A handbook for researchers by Research Design Service London. 2014:1–40. http://www.rds.nihr.ac.uk/wp-content/uploads/RDS-PPI-Handbook-2014-v8-FINAL.pdf;
Manning, J. C., Hemingway, P., & Redsell, S. A. Survived so what? Identifying priorities for research with children and families post-paediatric intensive care unit. Nursing in Critical Care, 2017;23(2):68–74. https://doi.org/10.1111/nicc.12298).
Janvier, A., Bourque, C. J., Dahan, S., Robson, K., & Barrington, K. J. Integrating Parents in Neonatal and Pediatric Research. Neonatology, 2019;115:283–291. https://doi.org/10.1159/000492502

1.2 Reviewer comment: For me, it is not clear whether this effort to consult parents and clinicians about the study design and study materials was part of COLLABORATE from the beginning. You mention this under 'Patient and Public Involvement'; 'At this preliminary stage of the development of COLLABORATE', so I guess it is part of total design?

Response: The PPI consultation which involved parents and clinicians that we relate in this manuscript has been conducted at the beginning of COLLABORATE. The COLLABORATE protocol has not been finalised, and this consultation was carried out as an initial step in development. We will incorporate PPI activities and consultations throughout the study.

1.3 Reviewer comment: As a former nurse on a NICU I always regret that no nurses were involved in the clinical participants group, but it is what it is. I see that 'Patient 1' is also Paediatric nurse. So there is a chance that experiences of nurses are involved. I know that for successful trial execution on the ward a study-team that also includes nursing representation is important.

Response: We agree with reviewer. We approached all healthcare professionals, including nurses but obviously were only able to include those that responded in our focus groups. We aim to explore methods to encourage nurses to put forward their views as part of the overall PPIE strategy of our group. Aside from this response, we would welcome a conversation with the reviewer in this regard.

1.4 Reviewer comment: I wonder what is done with the 'no' (table 1) and the 'unsure' of support for this trial. Why did they have these opinions and what is done to overcome this?

Response: The 'no' respondent was the mother of a baby who passed away during neonatal care and was disinterested in participation in trials in general. The 'unsure' participant felt that formula increased the chances of getting necrotising enterocolitis, even though current evidence is unclear. In response to the concerns of these participants, we plan to emphasise in the information provided that the justification for a trial is that the evidence-base is unclear. We also emphasise in study information that the COLLABORATE comparators are accepted practices throughout the NHS and not new treatments. Finally, it is important to note the purpose of the PPI work is not to persuade parents to participate, but to gain a deeper understanding of their thoughts and concerns.

1.5 Reviewer comment: I do not really understand the quote about theme 1, the consent process. Maybe because I am not a native speaker… 'families don't go there' and 'forget to fill out'. That refers to informed consent I presume? That families do not give consent because they forget?

Response: Yes, the speaker is stating that parents 'forget to fill out' consent forms. In saying that 'families don't go there', they mean that parents are emotionally unable to consent at the moment during NICU care. We have added the following to this section for further clarity: (Page 8, Line 48)

"…I appreciate the opt-out allows a much larger number of people, and often families don't go there. Not because they don't necessarily want to do it, but for whatever reason they have…they're not thinking about it or they read [the consent form]…and forget to fill out..."

1.6 Reviewer comment: I consider the consent procedure an important element of this study and see only one quote mentioned in the table/text.

Response: We found that participants offered only brief feedback and discussion on the consent procedure itself, if any at all. We have thus chosen to include their thoughts as an explanation of the socioemotional context in which the consent process occurs.

1.7 Reviewer comment: It is good that you could adapt the written information to parent responses, having a short and longer information form is very important. I wonder if you also constructed a script for the verbal message to parents. It is clear that neonatologists have doubts about the implementation of the study and this help for the conversation might help.

Response: This is a very helpful suggestion, thank you. We will develop a verbal script to assist clinicians in explaining the nature of opt-out as well as the rationale for the study.

1.8 Reviewer comment: I wonder if you have also established a 'Patient Advisory Board' or something like that to ensure involvement throughout the project. The quotes under theme 3 seem to say that this is possible and helpful 'this is what we are trying to do together' and 'to approach parents in really collaborative way'.

Response: Yes, indeed we are. We are in the process of establishing Patient Advisory Boards in addition to the inclusion of parents in Trial Committees. We agree the quotations you cite reflect participants' willingness to continue their involvement throughout the study.

1.9 Reviewer comment: The abstract section with results mention that there is a desire for research to be a partnership between clinicians, parents, researchers. I would appreciate more information in the discussion whether this has succeeded and which effects this has for the COLLABORATE study.

Response: This is a journey. COLLABORATE is still in its formative stages, and we certainly feel this has

been the case thus far. The outcomes of our approach have influenced the patient information sheet, and study design, and has grown the interest and involvement of clinicians and parents.

1.10 Reviewer comment: I very much agree with opt out in this context but for me, one reason for opt out given in the discussion 'an ongoing consent process', begs more explanation. Of course, 'opt-in' can also be organised as an ongoing process if you ask participants regularly if they still consent?

Response: We agree that ongoing consent processes are not exclusive to opt-out and that opt-in can also be organised as an ongoing process by regularly asking participants if they still consent. This statement was meant to clarify that the opt-out consent will be conducted in an ongoing format, to assure the same rights and flexibility to parents of participants as provided with opt-in. To further clarify this, we have adjusted the following text in the discussion section: (Page 11, Line 17)

"We have also shown that opt-out, as with opt-in consent, can be viewed as…"

1.11 Reviewer comment: I guess that no specific outcome-measures were added to the study on the basis of this consultation but it is possible that this is done after such a consultation. Same for the design of the study. That has not been adapted on the basis of this consultation.

Response: The reviewer is correct that we have not added any outcome-measures to the study based on this consultation. This is because we include outcomes identified in our previous work with a broad range of stakeholders including parents and former patients to develop a neonatal core outcomes set (Webbe et al. Core outcomes in neonatology: development of a core outcome set for neonatal research. Arch Dis Child Fetal Neonatal Ed. 2020 Jul;105(4):425-31).

1.12 Reviewer comment: For me, a message in the 'Key messages' under 'What is known' would also be that involvement increases recruitment rates.

Response: The reviewer is correct that involvement increases recruitment rates, (e.g. Greenhalgh et al. "Frameworks for supporting patient and public involvement in research", 2019). We considered including this but felt that the insights offered by our participants support more ways of improving the consent experience and creating inclusive recruitment and consent methods than only increasing numbers of recruits.

1.13 Reviewer comment: I am unsure about the first point under 'What this study adds': 'CER can help'. I do not know if patient involvement is standard in CER. If it is, then it 'CER helps'. If it is not, you can add an item: CER should also involve parents/patients.

Response: Our view is that PPI involvement should be standard in any research, and comparative effectiveness research is no exception.

1.14 Reviewer comment: The last point under 'What this study adds': 'understand and address their biases that inhibit trial participation'. It has potential to do this but has it also had an effect for COLLABORATE? I hope so, that would make the chances of the project to be successful larger.

Response: We hope that it has! Certainly, it has helped us in developing study design and information materials.

Reviewer #2
2.1 Reviewer comment: I would have a preference for input from more nursing and speech and language healthcare professionals in the clinician focus groups to gather input from ALL professionals involved in providing nutrition support in the Neonatal Unit in addition to a more evenly distributed gender balance.

Response: Please see response 1.3 above. We invited the involvement of all healthcare professionals.

Reviewer #3
3.1 Reviewer comment: Introduction: I main suggestion. add a paragraph about PPI that can be linked

to your project/consultation aim. You have a very brief PPI section in the methods which should stay their. Suggest to use references such as the NIHR – INVOLVE national guidelines that are important to share among other paediatric researchers.
(Examples to look at PPI introductions: Fiori M, Endacott R, Latour JM. Public involvement in designing a study on patient-witnessed cardiopulmonary resuscitation in hospital. Nurs Crit Care. 2020;25(5):313-320. doi: 10.1111/nicc.12429.; Manning JC, Hemingway P, Redsell SA. Survived so what? Identifying priorities for research with children and families post-paediatric intensive care unit. Nurs Crit Care. 2018 Mar;23(2):68-74. doi: 10.1111/nicc.12298.)

Response: We agree that it is helpful to connect our PPI consultation aims to extant literature and perspectives. Please see response 1.1 above.

3.2 Reviewer comment: Methods (first paragraph): please explain the number of PPI advisers that have been recruited. This is unclear. You did 6 focus and semi structured interviews with how many ex-patients and parents? Is the 6 focus groups correct as you had 9 volunteers (as described in Results). Thus were most 'focus groups' with only 1 volunteer (which should be an interview and not a FG? Please revisit this and add the number of volunteers in this section. Also, how many FG did you do with clinicians? (There were 11 volunteers of clinicians; all in 1 FG?).

Response: We have made the following edits to the methods section to answer the reviewer's questions: (Page 5, Line 37)

…through a national webinar. In total, twenty volunteers; ten clinicians, seven parents, two former patients, and one parent/former patient; participated in virtual focus groups or semi-structured interviews [16, 17]. Sessions with single participants utilised the same topic guide.

3.3 Reviewer comment: Methods (second paragraph): please provide detail of the qualitative analysis strategy. This is unclear. In the abstract it is stated Thematic Analysis (TA) but in the methods section it is not mentioned. Depending what TA strategy you opted to do, you need to described the steps of the qualitative data analysis. (Perhaps visit some of the most used TA papers by Braun and Clarke: Braun V, Clarke V. Successful Qualitative Research, a Practical Guide for Beginners. London, UK: Sage Publications Ltd; 2013; Braun V, Clarke V. Using thematic analysis in psychology. Qual Res Psychol. 2006;3:77-101.)

Response: We have made the following adjustments to the methods section to clarify our thematic analysis methods: (Page 5, Line 55)

and conducted interviews. WL and BM analysed all qualitative data using Framework Analysis. [20] Initial themes and concepts were identified through reviewing the data, then used to construct a thematic index and assign an index label to each phrase or passage of the transcripts. [20] The labelled raw data was then summarised and synthesised into the thematic charts to facilitate systematic exploration of the range of views, both between cases and within cases, to produce both descriptive and explanatory accounts of the data. [20] Data were organised and analysed using NVivo, version 1.0 (QSR International) [21].
(Page 14, Line 22)
Ritchie, Jane; Spencer, Liz; and O'Connor, William. "Carrying out Qualitative Analysis" In: Ritchie, J., & Lewis, J., eds. Qualitative Research Practice: A Guide for Social Science Students and Researchers. Thousand Oaks, CA: Sage Publications 2003:170-198.

3.4 Reviewer comment: Methods: although PPI consultations do not need ethical approval (your participants are volunteers and not study participants), I can I suggest to add this in the methods section and refer to the NIHR-INVOLVE guidance. Some researcher/readers might be sensitive about this.

Response: We have added the following section: (Page 13, Line 27)

"Research ethics approval for PPI consultations is not required [9]. However, we approached parents and former patients through the neoWONDER group that has agreed to be invited to participate in

consultations (REC reference: 20/yh/0330).

NIHR INVOLVE. Patient and public involvement in research and research ethics committee review. NIHR. Version 1. 2009. https://www.invo.org.uk/wp-content/uploads/2011/12/INVOLVENRESfinalStatement310309.pdf. Accessed 5/2021.

3.5 Reviewer comment: Also, I see at the end of the manuscript that the volunteers were approached via the neoWONDER project with a REC number. However, the PIS is about a study on linking existing data to evaluate long-term health and wellbeing of preterm babies. Perhaps this needs to be changed to reflect the issue that a PPI consultation is not a study and thus no ethical approval is needed according to the UK national guidance.

Response: Please see 3.4 above.

3.6 Reviewer comment: Results: Table 1 might need some explanation. What does 'position attributing knowledge' and support for trial' means. What, why and how what this data collected?

Response: We have changed the column label from 'position attributing knowledge' to 'reason for interest in participating' for clarity: (Page 6, Line 30)
"Reason for interest in participating"

3.7 Reviewer comment: Results: Page 7 lines 12-13: Suggest to describe in the text the named themes that belong to parents/patients and clinician and the one that is combined.

Response: We agree with the reviewer and have replaced the current text on Page 7, Lines 12-13 with the following text: (Page 7, Line 12)

"We identified three parent-patient themes; "pressure to breastfeed", "consent process", and "emotional trauma"; one clinician theme, "equipoise and personal beliefs"; and one theme combining parent-patient and clinician discussions, "collaboration and inclusivity."

3.8 Reviewer comment: Results: the description/presentation of the themes. The quotations used in the text need to have a reference to the participants between brackets so this can be linked to the Table.

Response: We have removed Table 2 and included the following descriptors to accompany each quotation in the results section:

(Page 8, Line 25-26)
"…my mum will share with me that she cried with her breasts bleeding, trying to express because she was told it was the best... And she had a woman sitting next to her in the expressing room who had, you know, 500 mils of milk sitting there…and this woman was saying, 'Oh, it's not enough.' My mum was like, 'you're kidding me. I've got five ml from the last four hours. And I'm bleeding into it. (NICU patient born at 28+4 weeks, now a paediatric nurse)"
(Page 8, Line 33)
"I remember when they talked about putting him onto formula, I said to the consultant, 'I'm really, really worried about him getting NEC [necrotising enterocolitis]. I'm really worried.' Cause I had it and…I know how bad it is…they assured me that the risk with formula was just as high as it was with donor milk. So I was like…if they need to gain weight and it's such a balancing act, isn't it?...I suppose it's the same for the doctors. They're just trying to balance the best options. (Mother who had NEC as a preterm baby, whose baby was born at 29 weeks) "
(Page 8, Line 40)
"… And at the end of the day, it has to be what's best…for your circumstances and what's best for your baby because your mum's milk is best, but if mum's milk is not available… you shouldn't make mums feel as if they're kind of a failure. (Mother of twins born at 29+5 weeks)"
(Page 8, Line 48)
"…I appreciate the opt-out allows a much larger number of people, and often families don't go there. Not because they don't necessarily want to do it, but for whatever reason they have…they're not thinking about it or they read [the consent form]…and forget to fill out...(Mother of a preterm baby who had

NEC)”
(Page 9, Line 16)
“I've never heard of that before… (Mother of twin boys born at 22 weeks, one of whom did not survive)”
(Page 9, Line 25)
“survivors and clinicians…(Mother of twin boys born at 22 weeks, one of whom did not survive)”
(Page 9, Line 36)
“I think this whole thing about us having to approach parents in a really collaborative way around the importance of…feeding…managing their expectations and their understanding of what is happening with that baby's gut, and that we're trying to help promote a healthy gut, not just for the time when they're in their unit, but beyond that time as a healthy gut for life – here is the one of the fundamental things that's going to influence their feeding for not just weeks, but months and years to come. (Neonatal clinician)”
(Page 9, Line 51)
“…I had this baby ripped from me…I didn't see her after birth. It was horrific…her first nappy was changed by somebody else... All her cares were done by somebody else. The first person she saw was somebody else…(Mother of a preterm baby with NEC)”
(Page 10, Line 4)
“…so little time…(Mother of a baby born at 33+3 weeks, pharmacist)”
(Page 10, Line 8)
“…leaflet front to back…(Mother of a preterm baby)”
(Page 10, Line 13)
“I'm the sort of person that likes to know everything, so I would want to read every tiny little detail of everything…but I know from speaking to other parents in the neonatal unit that a lot of parents…don't want to be involved as much and they don't want to know things. (Mother of a preterm baby who had NEC)”
(Page 10, Line 27)
“On a ward round, one negative sentence, a loose comment about something … just spoils everything. We try to police that to some extent [and] share all our anxieties and disagreement beforehand ….we have our own personal agendas or personal biases but keep them to ourselves when we are … in front of other people. that's where I see the issue about [a] unit that's sort of consenting to participate, but not then sticking to the protocol…and then bringing some of their own ideas into the consenting … [and] recruitment process (Neonatal clinician)”
(Page 10, Line 46)
”…we still haven’t got the answer (Neonatal clinician)”

3.9 Reviewer comment: Results: quotations; I noticed that most quotations in the text are coming back in the Table too. This questions the richness and in-depth of the focus groups / interviews. Are you using only 11 quotations (Table 1) to define the themes? Possibly you need to revisit the qual data and see if you have more in-depth narratives. Although this is not a qualitative study, your volunteers deserve that you handle their data with respect and use it according to the qualitative research methods (as you are using the COREQ guidelines).

Response: We have verbatim transcriptions of all participants’ contributions, and drew on this body of data in its entirety in order to extract themes. 11 of the most salient and illustrative quotes have been chosen from the wider set, in order to comply with the word limit of the journal.

3.10 Reviewer comment: Discussion: first sentence ‘Out study”. See my comment nr 4… this was not a study, this was a PPI consultation. If you call it a study, we need to see the ethical approval (at least from the University). Suggest to start with; This PPI consultation with…. Also; revisit the full manuscript regarding this issue; including the Acknowledgments as you called there a ‘pre-study’ which is not the case… it remains a PPI consultation that you report here. And wording like page 12 line 12: ‘Our research has identified…”. Again, I think you are not reporting a research project here.

Response: We have added: (Page 10, Line 50)
“This PPI consultation with”

(Page 11, Line 5)
“this consultation”

(Page 11, Line 23)
"by consultation participants"

(Page 12, Line 12)
"this consultation"

(Page 12, Line 16)
"This consultation"

(Page 12, Line 27)
"this PPI consultation for the"

3.11 Reviewer comment: Discussion: Good to see the sections related to the changes you made in the proposed trial. However, the discussion might benefit from some PPI references performed in the same or other field to highlight the importance (and benefits) of PPI consultation at the early stages.

Response: We agree with the reviewer's comment that PPI references could highlight the importance of PPI consultation. We have added the following clarifying statements and references to the discussion section: (Page 11, Line 9)
The methodology around PPI consultations continues to evolve. [23] Utilising PPI consultations in a study's early stages can assure relevance for patients and parents in the study's recruitment methods, ethics application, research protocol, and outcomes.[8] Our group illustrated an example of PPI consultations to identify a core outcome set for neonatology through consensus meetings around stakeholder viewpoints.[4] Others have called for "integration" of parents in research by frequently inviting their feedback.[14]
Ocloo J, Matthews R. From tokenism to empowerment: Progressing patient and public involvement in healthcare improvement. BMJ Quality and Safety, 2016; 25:26–632. https://doi.org/10.1136/bmjqs-2015-004839
Fiori, M., Endacott, R., & Latour, J. M. Public involvement in designing a study on patient-witnessed cardiopulmonary resuscitation in hospital. Nursing in Critical Care, 2020;25:313–320. https://doi.org/10.1111/nicc.12429;
Janvier, A., Bourque, C. J., Dahan, S., Robson, K., & Barrington, K. J. Integrating Parents in Neonatal and Pediatric Research. Neonatology, 2019;115:283–291. https://doi.org/10.1159/000492502. "
(Please note that Webbe at al 2017 is already cited in the manuscript).

VERSION 2 – REVIEW

REVIEWER	Reviewer name: Dr. Jos Latour Institution and Country: University of Plymouth, School of Nursing and Midwifery, Faculty of Health and Human Sciences Competing interests:None
REVIEW RETURNED	26-May-2021

GENERAL COMMENTS	Thank you the revisions which has increased the quality of the manuscript. Two suggestions: 1. In the introduction section, I suggest to move the sentence "Our aim at this preliminary stage was to involve parents, former patients, and clinicians in trial development." at the end of the last (new) paragraph. This would make the flow better ending the introduction section with the aim. 2. Methods last paragraph, I noticed that, suddenly, now you used Framework Analysis and not, as in the first version, "inductive and deductive thematic analysis". This is a bit odd to change leaving me to question your analysis strategy. Also, in the abstract it is still listed as 'inductive and deductive thematic analysis'. Can I suggest to describe clearly the analysis strategy and be consistent in reporting this also in the abstract.

	Once again, thank you for reporting this important part (and start) of your COLLABORATE study and wishing you a very successful trial. Looking forward seeing the outcomes.

REVIEWER	Reviewer name: Dr. Eric Vermeulen Institution and Country: VSOP Dutch patient association for rare and genetic diseases. Soest, The Netherlands. Competing interests: None
REVIEW RETURNED	23-May-2021

GENERAL COMMENTS	I thank the authors for their responses to the reviewers comments and agree with the changes in the paper.

VERSION 2 – AUTHOR RESPONSE

Manuscript ID bmjpo-2021-001112.R1 - "Incorporating parent, former patient, and clinician perspectives in the design of a national UK double-cluster, randomised controlled trial addressing uncertainties in preterm nutrition"
Word count: 2981/2500
Abstract 261/300

REVIEWER COMMENTS:
Reviewer #2
2.1 Reviewer comment: In the introduction section, I suggest to move the sentence "Our aim at this preliminary stage was to involve parents, former patients, and clinicians in trial development." at the end of the last (new) paragraph. This would make the flow better ending the introduction section with the aim.
Response: We have moved the following text to the suggested paragraph (Page 5, Line 40):
"...survivors and families [13, 14]. Our aim at this preliminary stage was to involve parents, former patients, and clinicians in trial development."
2.2 Reviewer comment: Methods last paragraph, I noticed that, suddenly, now you used Framework Analysis and not, as in the first version, "inductive and deductive thematic analysis". This is a bit odd to change leaving me to question your analysis strategy. Also, in the abstract it is still listed as 'inductive and deductive thematic analysis'. Can I suggest to describe clearly the analysis strategy and be consistent in reporting this also in the abstract.

Response: Framework analysis as described by Ritchie and Lewis is a type of thematic analysis. It focuses on identifying salient themes in raw data through use of a "framework." We agree that our Methods section and Abstract would benefit from clarification as to our methodology. We have made the following clarifications to the abstract (Page 3, Line 18):
"...Framework Analysis, a specific methodology within Thematic Analysis.
We have also made the following clarifications to the Methods section (Page 6, Line 14):
"... Framework Analysis, a specific methodology within Thematic Analysis.[20] Initial themes and concepts were identified through iterative review of the data, then used to construct a thematic index, or "framework", and assign an index label to each phrase or passage of the transcripts.[20] The indexed and labeled raw data was then summarised and synthesised into thematic charts to preserve the data's context while facilitating systematic exploration. These thematic charts produced salient themes, which serve as descriptive and explanatory accounts of the data.[20]