Author’s response to reviews

Title: Research involving adults lacking capacity to consent: a content analysis of participant information sheets for consultees and legal representatives in England and Wales

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Author’s response to reviews:

We would like to thank the reviewers for giving their time to review our manuscript, and for their very helpful and encouraging comments. The reviewers commented that it was an interesting and useful paper, and raised some points that required further clarification. We have revised the manuscript to address their comments in full and believe that this strengthens the manuscript ready for resubmission.

Reviewer #1: Dear Authors,

Thank you for submitting this interesting paper for review. You describe the investigation of an important and rarely examined aspect of clinical research practice.

Generally, your paper is well written. However, there are sections that require revision to make them more concise and to make your intended meaning clearer. The discussion in particular requires significant revision to make it clear to the reader why your findings are important and relevant. There appear to be some errors in terms of your presentation of numerical data. I also have concerns about your study classification system.

Please see my detailed comments below:
Abstract: Results section final line: "a small number inaccurately interpreted the law" - it is not very clear to what you are referring; do you mean a small number of studies? It may also be helpful to actually specify the number of studies rather than write "a small number".

Authors’ response: This has been amended to state “a small number of studies”. The number of studies has not been included, which is consistent with the narrative form used in the rest of the abstract. The numbers have been added throughout the main results section, as per later comments.

P1 Line 13: "they" - please revise to make it clear to whom you are referring.

Authors’ response: This has been amended

P1 Line 24: "a professional to act as a nominated consultee" - I am not aware that the MCA has this provision. Could you please provide a reference to the appropriate section of the MCA?

Authors’ response: Section 32(2) of the Mental Capacity Act states that if a personal consultee cannot be identified then someone who is prepared to be consulted but has no connection with the project should be nominated by the researcher. The Department of Health (as then named) ‘Guidance on nominating a consultee for research involving adults who lack capacity to consent’ states that “while someone with a professional relationship to the person lacking capacity must not be a personal consultee, it does not bar them from being the nominated consultee. It is therefore possible that a member of the care team or the GP of the person who lacks capacity could act as the nominated consultee” (p.8). The Clinical Trial Regulations has similar provisions for the legal representative to be “the doctor primarily responsible for the medical treatment provided to that adult, or a person nominated by the relevant health care provider”. The references have been added. This is a relatively common practice (additional research is underway to review current practice), although not well documented in the published literature

P2 Line 37: "never had decision-making capacity" - I would reconsider this phrase. It suggests that mental capacity is global or generic rather than time and decision-specific, as stated by the MCA. How could we ever know if someone "never had decision-making capacity"?

Authors’ response: Thank you for raising this point. The terms were intended to describe the significance of the different circumstances under which proxy decisions are made, i.e for those who have and have not held relevant views and preferences that can be used by proxies when making decisions that are intended to represent that person’s views and preferences. This is distinct from those who might have held such views, but never expressed them (or the proxy was
not aware of them). This has been amended (p2 lines 38-39), and please see comments on the similar point below

P2 line 48: Ref 17 - I think a page ref would help here.

Authors’ response: Thank you, we agree that would be helpful and a page reference has been added

P3 line 52: "examining the content empirically" - I am not sure what you mean here; please consider revising this phrase to make it clearer.

Authors’ response: This sentence has been removed

P3 line 58: I would consider changing "has" to "had".

Authors’ response: Thank you, this has been amended

P3 line 61: "frame of reference" - please explain what you mean by this phrase; consider revising it to make your meaning clearer.

Authors’ response: This has been amended to ‘The correct legal basis was determined by reference to the legislation governing research involving adults lacking capacity in England and Wales, the MCA and CTR.’ (p3 lines 63-65)

P3 line 61: "legislation"- please remind the reader what the legislation is and provide a reference.

Authors’ response: This has been added – see previous response

P3 line 67: Please change "National Institute of Health Research" to "National Institute for Health Research"

Authors’ response: Thank you, this has been amended
P4 lines 77-79: I think these categories are problematic. How was this classification system created? I am concerned that it is reductive and actually discriminatory to assign labels relating to mental capacity status to diagnostic categories. It certainly is not within the spirit of the MCA. Also, your use of terms such as "progressive loss", "sudden loss" and "no prior capacity" suggests that mental capacity is global or generic rather than time and decision-specific (see my earlier comments). Furthermore how does your system apply to people with multiple diagnoses? Please consider reformulating / relabeling this classification system.

Authors’ response: Again, thank you for raising this point. The categories are not intended to ascribe labels to individuals or groups of individuals who have received a diagnosis and/or experience impaired capacity. The search terms are those used by the NIHR Clinical Trials Gateway as categories of studies to enable users to search for trials in particular ‘conditions or disease areas’ (this is the term used by UK CTG) using these terms as search filters. This is described in the previous paragraph (p4 lines 73-75), however an additional statement about the nature of mental capacity has been added (p4 lines 73-75), and additional information about the use of the search term/condition has been added to Table 1.

P7 Table 1: "Care home(s)" - in relation to the comments above, many different types of people live in a care home and they are likely to differ in terms of their ability to make informed decisions. Please consider revising this.

Authors’ response: See later response regarding the prevalence of dementia in care home residents, and who lack capacity to consent to research (p18 lines 367-377)

P7 Table 1: I think the total no of CTIMPs included should be 6 not 9

Authors’ response: Thank you for highlighting – the number of CTIMPs is 9 (the figure above should have read 7 and not 4). This has been amended

P8 lines 151-154: please revise this long sentence to make it easier to read.

Authors’ response: This has been revised (p8 lines 156-159)

P8 line 157: "7-67%" - it is not clear to me from Table 2 how these percentages were derived.

Authors’ response: This has been added to Table 2 (p8)
P9 line 163: "nominated consultee or professional legal representative" - it may be helpful to the reader to explain who these people might be.

Authors’ response: This clarification has been added ‘member of the care team as a nominated consultee or professional legal representative’ (p9 line 168)

P9 line 167: "12 documents (29%)" - it says 13 docs and 31% in Table 2.

Authors’ response: Thank you for highlighting – the correct number is 13 (31%). The text has been amended (p9 line 171)

P11 line 202: "A number of the study documents" - please specify which ones.

Authors’ response: This has been added (p11 line 208)

P11 line 209: "when decisions are made" - I think it would be helpful to clarify that here you are talking about decisions about research participation for people who lack capacity to decide for themselves.

Authors’ response: This has been clarified ‘when decisions are made about research participation’ (p11 line 215)

P11-12 lines 214-223: these two sentences are very long and quite difficult to read; please break them up into a number of smaller sentences.

Authors’ response: This has been amended (p12 lines 223-227)

P12 lines 231-236: again, please break up this very long sentence to make the content easier to read.

Authors’ response: This has been amended to ‘The role of professionals acting as legal representative was sometimes extended to determining the person’s eligibility for the study, either explicitly (ID 19, ID 27) or implicitly by simply confirming that they understand ‘what the study involves, including inclusion and exclusion criteria’ (ID 30).’ (p12 lines 241-245)
P12 lines 236-238: this sentence does not make sense to me; please revise it.

Authors’ response: This has been amended to ‘Eligibility forms part of the investigator’s role; the role of the professional legal representative is to represent the person’s wishes and feelings as someone who is unconnected to the study.’ (p13 lines 246-247)

P13 line 252 "Inaccurate use of terminology" - I think it would be helpful in this section to inform the reader what the correct terms should be.

Authors’ response: This has been amended to ‘There were many instances of confusion in the use of the terms for the proxy, where they were called a ‘legal representative’ when the study did not fall under the scope of the CTR and therefore they should have been termed a consultee, or the term ‘consultee’ was used when the MCA was not the governing legislation and they were therefore acting as a legal representative.’ (p13 lines 264-265)

P13 lines 259-261: I agree that the term "assent" is not used in the MCA; however it is used by research professionals in relation to adults who cannot provide informed consent. It might be helpful to acknowledge this.

Authors’ response: This has been acknowledged ‘although it is a legally recognised term in paediatric research, and is used informally by some research professionals when referring to the involvement of adults who lack capacity to consent.’ (p14 line 272)

P15 lines 297-298: "The MCA clearly states...." - please reformulate this sentence, as it does not make sense as it is.

Authors’ response: This has been amended ‘The MCA clearly states that a person must be assumed to have capacity unless it is established that they lack capacity; this is a key principle of the Act’ (p15 line 310)

P15 Discussion: I think this section needs to explain more explicitly why the results you have obtained are important - what are the potential risks to participants and proxies and to research integrity if researchers don't get this right? It might be helpful to pick up some of the themes you alluded to in the introduction.

Authors’ response: This has been revised to link more explicitly to the importance of the risks (e.g p16 lines 318-324)
P15 line 318: "nomenclature and terminology" - do you need both words?
Authors’ response: This has been amended to ‘terminology’ only (p16 line 339)

P16 lines 321-323: "This risk of clarity.....who lack capacity" - it is not clear to me how the lack of clarity reinforces confusion and leads to exclusions - please make the links more explicit.
Authors’ response: The wording has been amended to “contribute to the confusion and lack of understanding about the legislation by health and social care professionals” and a reference added to support this (p17 lines 344)

P16 lines 327-345: these two paragraphs feel more like summaries of previously reported results or even new results, rather than a discussion of your findings - please revise.
Authors’ response: These paragraphs have been revised (p16 lines 349-365)

P16 lines 332-334: "care home residents..." - I think this sentence appears to suggest that care home residents are likely to have dementia. This may not be the case. I think it would be helpful to provide some data to back up this proposed association between living in a care home and having a dementia diagnosis.
Authors’ response: References have been added to support this statement ‘care home residents (ID 12, ID 13, ID 14) who may experience cognitive impairment associated with dementia which affects around 69% of care home residents [28], with a similar proportion who lack capacity to consent to research [29], and who may be particularly subject to fluctuation and variation in decision-making capacity compared to the populations included in other studies [30]’. In line with later comments, this section has been revised (p18 line 367)

P16 lines 339-342: this sentence is very long and difficult to follow; please revise it.
Authors’ response: This sentence has been divided (p17 line 361)

P17 line 360 "if that had not been met" - I am not sure what you mean by this; please revise this phrase.
Authors’ response: This sentence has been amended to ‘Studies consistently failed to address the complex issue of how the proxy would be able to represent the person’s wishes and feelings if that had not been met while the person had capacity, or if such wishes had never been expressed.’ (p19 lines 394-395)

P17 line 361: "if the person had never had decision-making capacity" - please see my earlier comments about this problematic contention.

Authors’ response: See previous response

P17 line 362: "intractable questions under the requirements of the current legislation" - I am not sure the questions are intractable "under" the requirements; do you mean they are intractable due to the nature of the legal requirements?

Authors’ response: Thank you, this has been amended (p19 line 396). We now state ”These may be intractable questions due to the nature of the requirements of the current legislation.”

P17 lines 365-371: these sentences are difficult to read; please revise them to make their content clearer.

Authors’ response: This has been amended to “There appeared to be a disconnect between the conceptualisation of advance decisions under the MCA and the wording used in the documents, which was based on the HRA template information sheet [9]. This was seen both in terms of the scope, as the MCA provisions relate specifically to Advance Decisions to Refuse Treatment (ADRT) only [5], and that the negative orientation towards treatment options under the MCA means that an ADRT would be relevant only to studies involving the treatment that was being refused and not refusal of research in general.” (p19 lines 399-405)

P18 line 375: "Strengths and limitations" - I think this section could be edited to make it more concise.

Authors’ response: This section has been edited to make it more concise

P18 line 378: "primary strength" - why is this a strength?

Authors’ response: This has been removed
P18 lines 387-391: this is a very long sentence which is difficult to read; please revise it.
Authors’ response: This has been revised (p20 lines 423-425)

P18 line 393: "stratification of samples by the three groups of conditions" - please revise this phrase to make the meaning clearer. What are the samples?
Authors’ response: This has been removed

P19 line 396: "a small sample...were reviewed" - please change to "was reviewed".
Authors’ response: Thank you, this has been amended

P19 line 403: "never had capacity" - please see my earlier concerns about this categorisation descriptor.
Authors’ response: This has been removed

P19 line 418: "will add to the context of proxy decision-making" - could you be more specific? What exactly do you mean here?
Authors’ response: This has been amended to “will provide additional information about proxy decision-making for research, which is currently poorly understood” (p21 lines 459-460)

P20 lines 424-426: does this sentence describe a research or practice recommendation?
Authors’ response: Thank you for highlighting – the development of interventions is recommended. This is therefore a research recommendation. This has been clarified (p22 line 466)

P20: lines 438-445: what are these recommendations based on? Legal requirements? Or your opinion? Please explain where they come from.
Authors’ response: This has been amended to “To ensure compliance with the legal requirements, and following the principles of informed consent, information sheets should
include sufficient information to allow the proxy to understand why they are being approached and the basis on which they should make a decision” (p22 line 480)

P21 line 449: "consultees" - please see my earlier comment; I am not sure whether professionals can be consultees.
Authors’ response: Please see earlier response

P21 line 459: "the clinical and representation roles were conflated" - I don't think you've stated this observation previously. I would expect to see this first in the main body of the discussion.
Authors’ response: This was stated in the Results section (‘Extending proxy’s role to include eligibility’, and ‘Disconnect between information provided to professional and personal proxies’) and Discussion (the disparity between the documents provided to personal and professional proxies and their roles) but has been more explicitly stated for clarity (p18 line 386)

P21 line 460: "adequate information" - how would you define "adequate"? By which / whose standards? Please consider revising this.
Authors’ response: This has been revised to “Future research practice should focus on ensuring adequate information is provided to proxies in order for an informed decision to be made, and therefore comply with the legal frameworks” (p23 lines 511-513)

P22 line 468/14: "UK Clinical Trial Gateway" should be "UK Clinical Trials Gateway".
Authors’ response: Thank you, this has been amended

P22 line 481: "National Institute of Health Research" should be "National Institute for Health Research".
Authors’ response: This has been amended

P30 Additional file 1: Please explain all acronyms, e.g., ITU, CNS.
Authors’ response: This has been amended
P31 Additional file 1: "massive haemorrhage" - is this the exact phrase used in the study? It seems a little strange!

Authors’ response: The trial documents use the term ‘massive haemorrhage’ (widely recognised term, including by National Patient Safety Agency) however the term has been amended to ‘traumatic haemorrhage’ which is also used in the trial

P32 Additional file 1: "National Institute of Health Research" should be "National Institute for Health Research".

Authors’ response: This has been amended

Reviewer #2: I found this a very interesting and useful paper.

The authors selected studies to include on the basis of capacity status (no prior capacity, progressive loss of capacity, sudden/acute loss of capacity), and also categorise studies into CTIMP or non-CTIMP type studies. Is it possible to include additional reflection on any similarities or differences in the key themes between these types of study?

Authors’ response: The heterogeneity of studies (type, population, context-setting, and condition) means that unfortunately the numbers of similar studies are too small to reflect meaningfully on the similarities and differences. The key differences are the type of proxy (personal or professional) and, to a lesser extent, whether it is in an acute or long-term setting. These are already reflected in the paper.

There is discussion of the consent form (starting line 272) - I wondered whether term "consent form" should be modified as the proxy is not giving consent, but being consulted.

Authors’ response: This has been amended to clarify that this was specific to two CTIMPs (and hence were consent forms) (p14 line 382)

The authors are very clear that frame of reference is legislation governing research involving adults lacking capacity in England and Wales. The legislation differs in Scotland, and it would be helpful for the authors to clarify that the PILs included in the review were those written for recruitment in England and Wales and not for recruitment in Scotland. If any of the PILs were
aimed at recruitment in Scotland, then some of the terminology around "consent" may have arisen from PILs written for studies recruiting in Scotland.

In additional file 1, the recruiting countries are listed as UK/EU/Other - given the differing legislation and terminology, the authors may wish to consider listing England/Wales and Scotland separately in this table.

Authors’ response: This has been clarified in the limitations section (p20 lines 441-444). Additional file 1 has been amended to clarify that ‘UK’ was the recruiting country listed in the UK CTG database, but the study was eligible if it recruited participants in England and Wales, but may have recruited in other areas of UK

Furthermore, the authors may wish to reflect on where the lead investigators were based (England/Wales or Scotland) as this may have influenced the terminology included in the PILs.

Authors’ response: This is an interesting point, however these studies were predominantly multi-organisation led studies where the investigators and clinical trials units were geographically spread across different areas. It would be difficult to discern where the study documents originated from, but were likely to be collaboratively produced and possibly ‘borrowed’ from another study/existing template

The authors present some examples of text describing how the proxy might approach decision making in table 3. Would they go as far as recommending some of these phrases as examples of good practice that others could utilise when developing PILs.

Authors’ response: These are examples of content, rather intending to be used as exemplars. There may be scope for further research to explore proxies’ information requirements and develop content that could be recommended for use. This has been added to the ‘Recommendations for further research’ section

On lines 362-364, the authors note that there is no template for clinical trials falling under the CTR - again, would they go further in recommending that such a template be developed (and if so, who should take responsibility for this?). They make a similar point on line 446, noting that further guidance is needed.

Authors’ response: We thank the reviewer for this suggestion and we have added the recommendation that a template be developed by the HRA, as they have developed existing templates (p22 lines 490-492)
The authors make an important point on line 444/445 about not increasing the length of study documentation. They may wish to consider the potential for a layered approach to providing this type of information.

Authors’ response: Thank you again for this suggestion. This is has been added to ‘Recommendations for research practice’ (p22 lines 486-489)