Author’s response to reviews

Title: CARer-ADministration of as-needed subcutaneous medication for breakthrough symptoms in homebased dying patients (CARiAD): study protocol for a UK-based open randomised pilot trial

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Dear Ms Cockayne

Thank you very much for the detailed feedback on our submission, it is much appreciated.

Re: checklist items.

In our team, we debated the level of detail which will be allowed under each of the checklist points, and clearly ended up summarising too severely in our first iteration. We have now added back what we hope is the required level of detail.

1. "Item 5b of checklist page 27 of the manuscript please give the name and contact details of the study Sponsor": This information has now been included, and is on page 29 of the amended version.

2. "Item 5c of the checklist page 27 of the manuscript, please include some additional text to clarify the role of the Sponsor": Additional information has been added to clarify the role of the Sponsor. This can be found on page 29.

3. "Item 5d of the checklist page 27 of the manuscript, please include some additional text to clarify the composition and role of the TSC": Additional information has been added to clarify the composition and role of the TSC. This can be found on pages 27-28.

4. "Item 21a of the checklist page 27 of the manuscript, please include some additional text to clarify the composition and role of the DMEC": Additional information has been added to clarify the composition and role of the DMEC. This can be found on page 28.

5. "Item 25 on the checklist: please confirm how important protocol modifications will be made subsequent amendments be sent to ethics": More detail has been added on how protocol modifications will be communicated to relevant parties, as well as steps towards implementation.

Re: Other points:

1. "Regarding the eligibility criteria, can you please clarify if any specific criteria will be used to assess:"
a. when a patient has entered the 'last weeks of life' and is likely to lose the oral route for medication

b. the carer's mental state, vision and physical condition

c. relational issues

d. a history of substance misuse in a family or is this purely a clinical judgement of a health care professional?

Thank you for raising this point. We have not been sufficiently clear in our first iteration. In the amended version, we have now indicated that it is based on healthcare professional judgement, and thus not based on the use of specific tools/criteria. (Please see page 13)

2. "Page 15 lines 9-12 will data entry staff be blind to group allocation?": No, indeed they will not be blind, and we have now added text to make this clear on page 15.

3. "Adverse event reporting. Can you please include a definition of an adverse event for this study; define the reporting period and if adverse events for both the patient and carer be collected and reported?": This detail has now been included on page 20.

I hope you find the changes in order.

Kind regards, and Happy New Year!

The CARiAD team