Author's response to reviews

Title: Alternative Forms of Hydration in Cancer Patients in the Last Days of Life: Study Protocol for a Cluster Randomised Feasibility Study

Authors:

Andrew Davies (adavies12@nhs.net)
Melanie Waghorn (melaniewaghorn@nhs.net)
Julia Boyle (j.boyle@surrey.ac.uk)
Ann Gallagher (A.Gallagher@surrey.ac.uk)
Sigurd Johnsen (s.johnsen@surrey.ac.uk)

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Dear Professor Altman,

Thank you for your email of 20th July with reviewer comments on the protocol entitled:

The comments were very helpful and we have addressed the concerns as follows:

1. The title has been changed as requested to ‘Alternative Forms of Hydration in Cancer Patients in the Last Days of Life: Study Protocol for a Cluster Randomised Feasibility Study’

2. The email addresses of all authors have now been included on the title page

3. The Methodology sub-section in the Abstract has been renamed ‘Methods/Design’

4. The consent statement in the Abstract has been moved to the Methods sections and it has been explained that written consent will be obtained from all patients or their designated consultee

5. Funding information has now been included in an Acknowledgements section at the end of the manuscript, before the reference list
6. Additional files have been explicitly referenced in the manuscript text and a list of Additional files with requested information has been included after the reference section.

Response to comments from reviewer Dr Ottevanger

Major Comments:

1. As this is a feasibility study in order to inform the design of a full randomised controlled trial (RCT) it was decided that hospitals and hospices would not be stratified for drugs used in pain therapy and terminal schedules. Instead the feasibility study is collating information on the drugs used by hospitals and hospices participating in the trial to assess whether this is an important factor in eliciting agitation. At present there is no consistent evidence that methadone worsens agitation and whilst steroids have been reported to cause agitation this effect is not common.

2. We agree with the reviewer that the frequency of terminal agitation is not well documented and the purpose of the feasibility study is to determine the number of patients required for an adequately powered RCT.

3. The statistician feels that it would be advisable to stay with two-sided testing as we don’t want to close our mind to the possibility that clinically assisted hydration might worsen terminal agitation

4. The adverse effects of clinically assisted hydration are described in the patient information sheet (Appendix 1). All adverse events, including those linked to the
administration of fluids (e.g. fluid retention or cannulation site problems) will be documented in the case report forms, this is described under the governance section on p15

5. The reviewer is correct in that the protocol is for a feasibility study which has been funded in order to provide data for the design of a RCT

Minor Comments:

1. LCP has now been fully defined at the point of first use

2. The volume of fluid to be administered is based on NICE guidance

3. As the trial is a feasibility study we felt it was important to replicate ‘real life’ and not to exclude patients with brain metastases. Data obtained from this feasibility study will be used to assess what stratification strategy should be adopted in the RCT. Our intention would not be to exclude patients from the research but to design a trial that controls for any patient disease status.

We hope that the changes made and our responses to the reviewer’s concerns are acceptable. We look forward to hearing from you shortly.

Yours sincerely

Dr Julia Boyle

[University of Surrey logo]