Author’s response to reviews

Title: Study Protocol: ASCRIBED: The impact of Acute SystematiC inflammation upon cerebRospinal fluid and blood BiomarkErs of brain inflammation and injury in Dementia: a study in acute hip fracture patients

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Author’s response to reviews:

See letter and below

Dear Editor
Thank you for your email and comments.

1. In the Methods as well as the Ethics approval and consent to participate sections please clarify whether consent will be sought in written or verbal form. If consent is to be verbal please justify this method over written consent and include a disclaimer that your ethics committee has explicitly approved the method of verbal consent.

We confirm the majority of consent was written but we had an option for witnessed verbal consent as below.

Our ethics approval for consent was as in the protocol:

Approaching patients pre-operatively

- Option 1: Where a patient has capacity to consent, we will provide study information and give patients as much time as is practicable in the situation to consider it. Patients will have the opportunity to ask questions and discuss the study. We will seek to take full written consent or witnessed verbal consent (in accordance with the Declaration of Helsinki, 2008; paragraph 22) at this point.

- Option 2: In cases where a patient declares they are unable to process the information and/or are assessed as not having capacity, a Personal Consultee (England, Mental Capacity Act, 2005) or a Legal Representative (either a welfare guardian, welfare attorney or nearest relative, Adults with Incapacity (Scotland) Act 2000) will be provided with study information. The personal consultee/legal representative will be given as much time as is practicable in the situation to consider the information, to ask questions and discuss the study. We will seek to take full written agreement (England) or consent (Scotland) from the personal consultee/legal representative at this point.

- Option 3 (England only): In cases where a patient declares they are unable to process the information and/or are assessed as not having capacity, should a personal consultee not be available, the research nurse will identify a professional consultee (Mental Capacity Act, 2005). The professional consultee may be a member of the team providing clinical care, but will not be a member of the research team. As in similar work of this type, this person may be the patient’s treating surgeon.

Approaching patients post-operatively

As appropriate, the research nurse will remind the patient of the study, reassess capacity (as required) and complete pre-consented study related procedures. From this point the following options emerge:
• Option 1: Where the patient has already given written informed consent, the research nurse will proceed with other study related procedures. Where the patient has consented verbally but not in writing, the RN will seek written consent. Where a patient has consented themselves pre-operatively and are assessed as having lost capacity post-operatively, the research nurse will continue with study procedures in line with the patient’s pre-operative wishes (as recorded on the consent form), unless the patient appears to object to any of the active study procedures (i.e. blood sampling and/or MMSE~2: SV). Should the patient appear to object, the RN will return one further time and if the patient still appears to object, the patient’s active involvement in the study would discontinue.

• Option 2: If agreement/consent was gained via personal/nominated consultee agreement (England) or legal representative consent (Scotland) and the patient is assessed as having capacity, the research nurse will: re-introduce/introduce the study, explain what has already happened in relation to study and why, and then provide information about what their continued contribution would involve. The patient will be given as much time as is practicable in the situation to consider the information, to ask questions and discuss the study. The research nurse will seek their full written informed consent.

• Option 3: If agreement/consent was gained via personal/nominated consultee agreement (England) or legal representative consent (Scotland) and the patient is assessed as still not having capacity, the research nurse will continue with relevant study related procedures, unless the patient appears to object to any of the active study procedures (i.e. blood sampling and/or MMSE~2: SV). Should the patient appear to object, the RN will return one further time and if the patient still appears to object, the patient’s active involvement in the study would discontinue. If a nominated consultee agreed pre-operatively and a personal consultee has emerged, the research nurse will engage with this individual as appropriate.

We have clarified in the participants section line 196 page 8, recruitment and consent procedures lines 248-249 page 11, as well as lines 277-283 page 12. We have included an explicit statement that ethical permission included witnessed verbal consent (Line 492 page 21).

2. In your Funding section, please also state the role of the funding body in the design of the study; collection, analysis, and interpretation of data; and in writing the manuscript.

We have adjusted this to indicate the funder had no role in the study at lines 510-512 page 22 in the funding section.

3. Please remove all information related to funding from the Acknowledgments subsection. Funding information should be presented solely in the Funding subsection. The Acknowledgments subsection should solely feature information which acknowledges anyone who contributed towards the article who does not meet the criteria for authorship including anyone who provided professional writing services or materials. We have removed the funder from the acknowledgment section lines 511-12 page 22.
4. In the Funding section please declare that the funding body provided peer review for your study. We have adjusted this to indicate the funder had provided peer review at lines 514-516 page 22 in the funding section.

Any queries please let me know.

Yours Sincerely

Professor G C FOX