

## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

### ARTICLE DETAILS

<b>TITLE (PROVISIONAL)</b>	Study protocol for enhanced CJD surveillance in the 65+ population group in Scotland: an observational neuropathological screening study of banked brain tissue donations for evidence of prion disease
<b>AUTHORS</b>	Peden, Alexander; Kanguru, Lovney; Ritchie, Diane; Smith, Colin; Molesworth, Anna

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Nobuo Sanjo Tokyo Medical and Dental University, Graduate School of Medical and Dental Sciences, Department of Neurology and Neurological Science
<b>REVIEW RETURNED</b>	26-Aug-2019

<b>GENERAL COMMENTS</b>	Dr. Peden et al. described their plan of a retrospective pathological screening study for CJD surveillance in the 65 years or older population in Scotland. The aim of the study is to establish for searching unrecognized prion disease in people aged 65 years and above in Scotland. They will conduct 5 kind of biochemical analysis methods, including western blotting and TR-CulC, as well as immunohistochemistry, and PRNP gene analysis. The plan of the study is accurate and precise, and expected for high sensitivity and specificity.
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<b>REVIEWER</b>	Francesca M Brett Department of Clinical Neurological Sciences Beaumont Hospital Dublin 9
<b>REVIEW RETURNED</b>	04-Sep-2019

<b>GENERAL COMMENTS</b>	Should you identify cases that have been 'missed' how will you approach this. Do you have CSF on the retrospective cases ? Have you any preliminary results
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### VERSION 1 – AUTHOR RESPONSE

Reviewer 1 appears to be happy with the manuscript.

Reviewer 2 asked "Should you identify cases that have been 'missed' how will you approach this". Our approach to dealing with missed cases is described in the sections entitled "Action for positive cases" (bottom of page 11), and "Statistical analysis" (page 13) and also in the area at the bottom part of Figure 1, labelled "Action for positive cases".

Reviewer 2 also asked: "Do you have CSF on the retrospective cases?"

We do not have cerebrospinal fluid (CSF) samples from the cases, because this is a neuropathological study of banked brain tissue donations from the deceased, which have been archived and made available for research. Neuropathological examination and investigation is the definitive means of prion diagnosis; CSF analysis would provide no additional information to answer the research question, even if samples were available for these cases, which they are not.

Reviewer 2 also asked: "Have you any preliminary results."

This is a study protocol paper and the results to this study will be reported in due course elsewhere.