Reviewer's report

Title: Exposure to General Anesthesia and Risk of Alzheimer's Disease: A Systematic Review and Meta-Analysis

Version: 1 Date: 8 August 2011

Reviewer: Fiona Matthews

Reviewer's report:

Undertaking epidemiological meta-analyses are very hard to undertake well and in general the authors have done a good review here. There are a few points that make some of their results less generalisable than they discuss.

In general what is presented is a good systematic review of the narrow hypothesis mentioned by the authors. I find this somewhat disappointing that a very clear and good quality review systematic is let down by the quality of the original question. However it appears as though the original question is not really the question at all. There is a difference between AD and dementia though the authors appear to interchange and swap the two.

Major compulsory revision

1. The use of terms for epidemiological investigations traditionally are poorly coded within the Bibliographic databases and can therefore lead to the exclusion of good epidemiological investigations. This may well be the case here.

2. The other factor is the use of just AD and the definition of AD used by the authors will be enormously restrictive of some of the largest epidemiological studies that have been used over a number of years. However many of the studies are just not AD but dementia. This needs to be clearer. It appears as though dementia was used, but AD is the hypothesis.

3. I do not understand all their results. Some are quoted as being calculated from the exposed cases and controls but they do not agree with the papers themselves. Why have the authors changed the results? This is particularly worrying where their results are now attenuated from the original papers. They have additionally highlighted odds ratios that agree with their ideas above other ones presented that do not. Why did the authors not discuss with the original study authors the best results to use?

4. Do any of the bibliographical databases mentioned by the authors cover the PsychInfo sets of journals, that include some very important papers that are not generally in Medline. [I'm afraid I do not know the google scholar reach].

Minor Essential revisions

5. The discussion of AD is simplistic at best and is not really the most up to date literature on AD that have been recently reviewed in a systematic way.
6. There is obviously a problem with individuals who are already well on a cognitive decline pathway who may not be offered the same opportunity for GA as individuals who are of normal cognition and this needs to be considered within the analysis.

Discretionary revisions
7. It is difficult to understand how a randomised controlled trial could be undertaken in this area. The risk of AD is low and the patient group that could be randomised is small.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that I have no competing interests