Reviewer's report

Title: The descriptive epidemiology of delirium in a large population-based cohort study: results from the Medical Research Council Cognitive Function and Ageing Study (MRC CFAS)

Version: 2
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Reviewer: Timothy Girard

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Davis and colleagues describe the results of a population-based cohort study within which they sought to identify delirium using the Geriatric Mental State (GMS) exam, examine the association of GMS-based delirium with mortality and dementia, and determine the age-based prevalence of GMS-based delirium. The authors conclude that the GMS-based delirium algorithm has criterion validity due to associations with mortality and dementia, but major limitations should not only be acknowledged (as the authors have done) but should also influence the language used throughout the manuscript, as I will describe in detail.

Major comments:

1. Page 2, Abstract - The authors base their study design and conclusions primarily on the premise that prediction of mortality and dementia demonstrate criterion validity. But, they also acknowledge in the first sentence of the Abstract that these associations have not been well established in the general population. A major limitation of the study is that the associations with mortality and dementia are not specific to delirium; numerous other factors may account for the associations, including the possibility that what was diagnosed as delirium was actually symptoms of early dementia. Though the authors acknowledge this limitation in the Discussion, much of the paper is not written in a manner influenced by how critical this limitation is. The diagnosis made is referred to as delirium in the title and throughout the manuscript, when a better description would be "delirium symptoms" since the current design did not allow for the diagnosis of delirium to be validated as specific.

2. Page 6, Statistical Analyses - The associated examined are very likely confounded by unmeasured variables. Only age, sex, and a subjective measure of severity of illness (which, as far as I can tell, has never been validated to accurately reflect severity of illness) are accounted for. The authors should discuss the possibility of confounding in the Discussion.

3. Page 7, Results - Nearly one-fourth of the sample had dementia at baseline. Please describe the sensitivity and specificity of this approach taken to diagnose dementia. How likely was it that mild cognitive impairment (which may lead to some of the symptoms characterized as delirium symptoms) or even frank dementia went undiagnosed at baseline? Is it possible that the symptoms of delirium are actually indicators of early dementia? Associations with mortality and
dementia could be taken as criterion validity indicators of MCI or early dementia just as well as of delirium. Couldn't the increasing prevalence of delirium with age be the result of symptoms of dementia being misdiagnosed as delirium?

4. Table 1 - To identify "acute change," the respondent is asked about confusion (which would indicate a change in cognition), but a change in consciousness is also required to diagnose delirium. As mentioned earlier, couldn't these symptoms all occur in the context of worsening cognition (without any disorder of consciousness) attributable to MCI?

Minor comments:

1. Page 3, Introduction - The phrase "inverse relationship" suggests that as predisposing factors increase, precipitating factors decrease, which is not necessarily the case. I believe the authors mean to say that in the setting of multiple (or severe) predisposing factors, fewer (or less severe) precipitating factors are required. Please clarify.

2. Table 1 - How was "sudden" defined? This could be taken as anything from a period of minutes to a period of weeks or even months.

3. Table 2 - It appears that almost everyone who had delirium died prior to the 2-year follow-up. Is this true? If so, how was the association with dementia demonstrated?

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

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests.