

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Does low-dose acetylsalicylic acid prevent cognitive decline in women with high cardiovascular risk? A five-year follow-up of a non-demented population based cohort of Swedish elderly women
AUTHORS	Börjesson-Hanson, Anne ; Kern, Silke; Skoog, Ingmar; Östling, Svante; Kern, Jürgen

VERSION 1 - REVIEW

REVIEWER	Robert Stewart Professor of Psychiatric Epidemiology and Clinical Informatics King's College London (Institute of Psychiatry) United Kingdom Statement of competing interests: I have carried out collaborative research in the past with some of the authors, although I do not feel that this has influenced my review.
REVIEW RETURNED	04-Jul-2012

GENERAL COMMENTS	The manuscript presents interesting findings, is well written and appears methodologically sound. The authors are appropriately circumspect about their findings. The only additional issue they might want to consider in the Discussion is whether, given that ASA use was associated with lower baseline MMSE, the association with reduced cognitive decline over the follow-up period might represent regression to the mean. I don't believe there is anything that can be done about this in a 2-wave study, but it might be worth mentioning.
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REVIEWER	Peter P. Zandi Associate Professor Department of Mental Health Johns Hopkins Bloomberg School of Public Health
REVIEW RETURNED	15-Jul-2012

GENERAL COMMENTS	This paper reports on data from two sister prospective observational studies from Sweden that suggest that compared to women non-users of low dose aspirin users did significantly better on the MMSE over two time points up to 5 years apart. The strength of the association was greatest for women who used aspirin at both the baseline and follow-up visits, and the associations did not change when incident dementia cases were removed. The strength was particularly apparent among women at high risk of cardiovascular disease by the Framingham risk score, although almost all the women in the combined cohort (~95%) were defined by this measure as at high risk. Results for other cognitive tests (word
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	<p>fluency, naming test and word memory) were similar but not significant, and there was no significant association with incident dementia.</p> <p>The relationship between use of low-dose aspirin and cognitive function over time is important. Many elderly individuals use low-dose aspirin for cardio-prophylaxis, and it would be helpful to know the neuro-cognitive effects of aspirin in order to better evaluate the risk-benefit ratio of its long-term use among elderly. The use of daily low-dose aspirin is established for secondary prevention of cardiovascular disease, but its use for primary prevention among those at high risk is less clear .</p> <p>The authors do a good job of reporting the findings from this study and discussing the strengths and limitations of the study and placing the findings in the context of existing literature. And the study does have certain strengths – the prospective design, representative sample, and use of the Framingham risk score to look among women at high cardiovascular risk.</p> <p>However, the study has other limitations as well that diminish the overall impact of the findings. The study sample is relatively small, and the findings are only with the MMSE over two time points which is not a particularly sensitive measure of cognitive change over time. The authors discuss these limitations, but they should add the possibility that the findings could be due to chance.</p> <p>I have just a couple other suggestions for the authors.</p> <p>In the results, the authors report that the MMSE declined between the 2000 and 2005 examinations. It would be helpful to know by how much on average over the whole sample, among aspirin non-users, and among aspirin users (without controlling for any other covariates)</p> <p>The current formatting of the tables, especially Table 1 and to a lesser extent Table 3, is difficult to read and should be cleaned up. The rows are not aligned so it is difficult to read across the table.</p> <p>And in Table 2 it would be helpful if the authors could clarify if the factors at the top of the table (ASA use at baseline, MMSE at baseline, Birth year, and GCVD score) were all included in one model. From the footnote it appears the Additional Factors were each added separately.</p>
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VERSION 1 – AUTHOR RESPONSE

Response to reviewer 1: Robert Stewart

Thanks for reviewing this paper and for your comment on the possibility that the reduced cognitive decline among ASA-users might represent regression to the mean, which we cannot exclude so we have now included this in this in the discussion (page 11).

Response to reviewer 2: Peter P Zandi

Thanks for valuable comments.

Without controlling for any other covariates the average MMSE decline over the 5-year follow-up

period was -0.88 for all included in the study; -0.95 for ASA non-users; and -0.05 for ASA users. This clarification is now included in the result section (page 8).

We have now formatted table 1 and 3 so they will be easier to read. For table 2 we have change the title so that will be more informative: "Multiple linear regression results of selected factors affecting change in MMSE in women followed from 2000 to 2005" and as may be more clear now: ASA use at baseline, MMSE at baseline, Birth year (was change to "Age at baseline") and GCVD score were all included in one model and than each other additional factor was added to the model separately. We have also corrected the footnotes.

In the discussion section we also added a few words on the possibility that our findings could be due to chance (page 11).