Author’s response to reviews

Title: Temporal trends in incidence, recurrence and prevalence of stroke in an era of ageing populations. A longitudinal study of the total Swedish population.

Authors:

Karin Modig (karin.modig@ki.se)
Mats Talbäck (mats.talback@ki.se)
Louise Ziegler (louise.dencker-ziegler@sll.se)
Anders Ahlbom (anders.ahlbom@ki.se)

Version: 1 Date: 10 Jan 2019

Author’s response to reviews:

Authors response: Thank you very much for reviewing our work and thank you for your suggestions and relevant feedback. We appreciate your careful review of our manuscript and hope to have adequately addressed all changes that were recommended. Please find our response to the specific questions and suggestions below.

Technical Comments:

Editor Comments:

BMC Geriatrics operates a policy of open peer review, which means that you will be able to see the names of the reviewers who provided the reports via the online peer review system. We encourage you to also view the reports there, via the action links on the left-hand side of the page, to see the names of the reviewers.

Reviewer reports:
Adesola Ogunniyi, MD (Reviewer 1): The authors have carried out a nationwide study of stroke incidence over 27 years and involving over 35 million subjects. The methodology is robust and the data well presented. However, it would be interesting to separate out ischemic and hemorrhagic stroke types to evaluate any differences.

Response: Thank you. We agree and have performed such analyses. Since around 80% of all strokes in old age are ischemic strokes, the figures presented in the manuscript correspond well to those of ischemic stroke. We have now added two figures as supplementary figures presenting incidence of first,
second, all and all recurrent strokes for ischemic and haemorrhagic stroke separately. We have further added some results about the two types in text in the manuscript and one more supplementary figure of the incidence rates for the two specific subtypes separately. In general, all results (i.e. trends) look very similar for the two different stroke subtypes, even if the levels differ.

The reasons for the declining stroke incidence rates were not satisfactorily discussed. Were there nation-wide health promotion efforts or were there changes in policy with regards to non-communicable diseases in Sweden during the study period. The reasons for the differences reported between European countries can also be speculated upon to make the discussion richer.

Response: Thank you. Even though the primary aim of this study was to explore and describe the incidence trends and not explain them, we agree that the discussion could be extended regarding this. A section with reflections on the reasons for the decline in stroke incidence from a Swedish perspective has been added to the Discussion (see below). The nation-wide health promotion efforts affecting stroke incidence in 1994-2014 were anti-smoking campaigns whereas campaigns to increase awareness of stroke came later, towards the end of the follow-up in our study.

The inserted section in the discussion:
Our results of declining incidence trends are further in line with those presented in a report from the nationwide Swedish Stroke Register, Riksstroke (22, 23). One of the main reasons for the declining incidence rates of first stroke could be the halved smoking prevalence until 2014, from just above 20% in the mid-nineties. From an international perspective, this is a large decrease and could be part of an explanation to the larger decrease in incidence in Sweden as compared to some other developed countries. Moreover, in the same period, a more aggressive primary preventive treatment of hypertension became part of the standard clinical practice in Sweden as in the rest of the Western world. Cerebrovascular disease is known to be strongly associated with hypertension (24) why this prevention strategy is likely part of an explanation to the declining incidence. The postponement of recurrent strokes on the other hand might well be the result of a more effective secondary treatment with platelet inhibitors and statins as well as a greater awareness of risks associated with atrial fibrillation with a subsequent increased search for atrial fibrillation in ischemic stroke patients and a more widespread use of prophylactic anticoagulant treatment.

Keiko Murakami (Reviewer 2): The objectives of this study were to investigate how the age specific incidence rates of recurrent strokes have developed in relation to the incidence rates of first strokes and how the postponement in age look like, and to see how the prevalence proportion of stroke as well as the absolute number of incident strokes has changed over time. Before accepting this manuscript for publication, the authors should consider the following.

1) The authors did not state the objective of this study in "Objective" of the Abstract section. (P.2, Line 3-10)

Response: Thank you, we have added this in the abstract.

2) Why did the authors allow for a 7 year wash-out period for identification of first strokes? Please show where the figure "7 year" come from, by citing some references. (P.5, Line 36-39)
Response: In order to estimate the first stroke event one would need information about the entire disease history of individuals, which is rarely available. When using administrative health registers there is a time point when the register starts resulting in left truncation, i.e., before a certain time there is no information about the disease history of individuals, meaning that it is not possible to definitely define a first occurrence of disease. A practical way to handle this is to apply a period at start where events are disregarded in calculations of disease occurrence and only individuals free of disease after the wash out period are followed up. As far as we know, there is no golden standards for how to define a first stroke using administrative registers, only praxis. A 7-year period was chosen because this is the period that the National Board of Health and Welfare use for their statistics about first events of myocardial infarction as well as for stroke. It is most likely chosen rather arbitrary from the beginning, but since the risk of recurrence is highest in the following year after the first event, and the fact that rather few individuals are either alive or did not experience a recurrent stroke 7 year after the first stroke (see new complementary figure below), the 7 year period is probably a valid time period for wash out.

We have explained this more thoroughly in the methods section now.

Complementary figure for reviewer only, competing risk analyses. The figure shows the proportion of individuals that are alive and stroke free up to 7 year after the first stroke, 30-35%. In older ages the proportion is much lower, for example in ages 85-89 years it is only 10-15%.

3) I think that the trends in Sweden may be somewhat different from those in other countries because standard of medical care is high in Sweden. Please mention it in brief in the Discussion section.

Response: It is possible that the trend in Sweden could be different from other comparable countries due to Swedish anti-smoking policies came early and were quite ambitious. A section on this and some general reflections on the reasons for the decreased incidence has been added to the Discussion.