Author's response to reviews

Title: Stroke prevalence in Spanish elderly from screening surveys

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Author's response to reviews: see over
Dear Sir,

We have followed in detail your indications for revising the manuscript *Stroke prevalence in Spanish elderly from screening surveys* according to the reviewers' indications. We attach the text indicating location of different comments and their answers.

Changes in the manuscript were done in the following sections and paragraphs:
ABSTRACT: 3rd paragraph.
INTRODUCTION: None.
METHODS: 3rd – 5th paragraph.
RESULTS: 4th paragraph.
DISCUSSION: General review
BIBLIOGRAPHY: Nine new references
TABLE 1: We add more information: type of sample, percentage collaboration and diagnostic criteria.

We thank you for your suggestions.

Thanking you in advance for your attention in this matter. Yours faithfully,

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Reviewer's report
Title: Stroke prevalence in Spanish elderly from screening surveys

Reviewer 1
Thank you for your interesting comments, the replies to which are to be found below.

Discretionary Revisions

Comment
In Spain, the most credible surveys of stroke seem to be door-to-door investigations involving screening. What other types of community-based studies were available (e.g., hospital-based surveillance efforts)? Why were they less credible?

Reply
There are other types of studies, e.g., based on hospital discharges. In general, such studies have tended to focus on stroke incidence. There are no other stroke prevalence studies (please see a recent review of this issue in: Medrano Albero MJ, Boix Martínez R, Cerrato Crespán E, Ramírez Santa-Pau M. Incidencia y prevalencia de cardiopatía isquémica y enfermedad cerebrovascular en España: revisión sistemática de la literatura. Rev Esp Salud Pública 2006; 80:5-15).

Comment
Why were different time frames used for the Spanish and non-Spanish studies?

Reply
We used temporal restrictions in research such as publication year (1985 to date) and added a comment on time frames. Prevalence years for Spanish and non-Spanish studies were different, ranging from 1991 to 2002 and 1987 to 2001 respectively.

Comment
Why was the Kungsholmen Study considered? That study had no screening phase (see Table 1).

Reply
A note to Table 1 and a comment in the Discussion section have now been added. While the Kungsholmen Study had no genuine screening phase, each individual was medically examined using a protocol, and a systematic question on preceding stroke was included.
Comment
No critical appraisals were provided of the studies that were included. Thus, results of unpublished studies are especially problematic (poor quality?). Data on participation rates of the various studies would be helpful. What about diagnostic criteria? One could at least comment on whether they were similar between studies. Why were stroke types not available (occlusive versus hemorrhagic)? Were type-specific data not collected at all? Or do they simply lack credibility?

Reply
The initiative for a review of Spanish surveys was based on knowledge about existing results not being reported due to the strong latencies between data-collection and reporting time usually seen in such studies. We established a rather strict data-collection protocol, including data quality. Unfortunately, a description of these variables was omitted in this report. However, percentage collaboration and diagnostic criteria have now been included in Table 1. Clinical classification of lesions underlying stroke has traditionally not been available in door-to-door studies because of uncertainties about diagnostic details of events that preceded the prevalence date, sometimes for decades. In general, diagnostic data were not collected from medical reports and therefore not detailed. In a few instances, stroke diagnosis was self-reported and not based on medical judgement based solely on self-reported symptoms.

Comment
Comparisons were made between urban, urban mixed, suburban, and rural areas. Are these terms defined in the paper? Could the lower prevalence in the rural area be an artefact? For example, how typical would it be for elderly stroke survivors in the rural area to move to an urban or suburban area to live with adult children or to take up residence in a chronic-care institution?

Reply
A description of the demographic classification has now been included. Rural populations had under 2,000 and urban populations over 10,000 inhabitants. Urban, metropolitan populations with high proportion of immigrants were denoted as suburban. An urban mixed category was used to identify former rural populations which had become urban in recent decades.
Comment
More could be said about the panel of experts that designed the data collection questionnaire. For example, were any or all of them authors of the paper?

Reply
As suggested, an explanation about the panel of experts has been added. A panel of experts -RB, JLB and JPC- designed a questionnaire for data-collection on the basis of different studies focusing on demographic, methodological, diagnostic, disability and epidemiological data, and resolved issues concerning the diagnostic classification of specific individuals.

Comment
More could be said about the European standard population. At least give a reference, if not a definition.

Reply
As requested, an explanation and a reference have been added. The European standard population (Atlas of Health in Europe www.euro.who.int/Document/E79876.pdf may 2006) was selected because its age distribution was similar to those of the study populations.

Comment
What would be the nature of the publication bias that is potentially resolved by including unpublished studies?

Reply
We have included approximately 5% more information on stroke prevalence than previously available. Prevalence in remote geographical areas may scarcely have been described, since clinicians active in small hospitals might have more difficulties in drawing up scientific reports than their colleagues in academic university teaching hospitals. Furthermore, the inclusion of unpublished studies might shed light on spatial variation of stroke occurrence in Spain where mortality due to stroke varies remarkably, increasing in the south. Unfortunately there were no stroke surveys conducted in such regions.
Reviewer’s report

Title: Stroke prevalence in Spanish elderly from screening surveys

Reviewer 2

Thank you for your interesting comments, the replies to which are shown below. As you will see, some new information has now been added to the text and certain aspects corrected. The English has been thoroughly revised and reviewed.

Major Compulsory Revisions

Comment
1. Although the logic of the paper is relatively well constructed, the writing of the paper can be considerably improved. There are numerous errors and writing mistakes in the text, which make it difficult to understand the ideas expressed. This occurs in most sections of the paper from the abstract, methods, to discussion. I suggest authors revise the paper carefully and let it be reviewed by an English editor. This can improve considerably the clarity of the paper, which at the moment has sections that are difficult to understand.

Reply
As suggested, the text has been revised in depth, possible problems areas duly identified and redrafted, and the English thoroughly reviewed by a native speaker.

Comment
2. The methods section of the paper is not complete, several sections are unclear, and overall it is difficult to get an impression of what was actually done in some cases. Examples include: a. Page 6, last paragraph starting A panel of experts: It is unclear what this paragraph is about. It is not clear about which panel of experts authors are referring to; authors refer to ADL, data-collection in Pamplona due to personal reasons. This paragraph seems not to fit in the paper.

Reply
On re-reading the text, we now realise that our explanations were perhaps too cryptic and this made the manuscript somewhat obscure and difficult to understand. Possible problem areas have now been identified, and the ensuing points better specified and/or clarified. A panel of experts -RB, JLB and JPC- designed a questionnaire for data-
collection on the basis of different studies focusing on demographic, methodological, diagnostic, disability and epidemiological data, and resolved issues concerning the diagnostic classification of specific individuals. This is a common procedure for classifying positive- or negative-screened individuals. The ill health of co-author, JMM, rendered data-collection in Pamplona unfeasible, and reported data were thus used instead. In fact, Dr. Manubens died of lung cancer shortly afterwards and the appropriate symbol for this is shown in the list of authors alongside his name.

Comment
b. Page 7, First paragraph starting Population and methodological it is not clear why demographic characteristics were obtained from the National Institute of Statistics, since individuals were actually interviewed. Is this referring to the sampling procedure? This is unclear.
Reply
Demographic characteristics of survey populations, relating to population concentration categories or immigration, were designed ad-hoc but correspond to terms used by the National Institute of Statistics (www.ine.es). An explanation to this effect has now been added to the text (page 7).

Comment
c. Are surveys representative samples of the regions? How were in general individuals selected, and what was the response rate of these surveys? Some of this information could be included, for instance in Table 1.
Reply
With some exceptions, they were not generally representative. As suggested, new information has now been included in Table 1, in the form of "Type of sample" and "Percentage collaboration".

Comment
3. The paper is relatively limited in terms of what the meaning or implications of the results are. In particular, the discussion section of the paper is not strong enough, as it is mostly focused on biases that could explain the results. Although this is important, authors do not make an attempt to explore what the possible causes of the geographical pattern could be, as well as the age and gender variations in stroke prevalence as observed. In order for this paper to be of interest to an international audience, authors will need to make a serious attempt to discuss what is behind the pattern that they observe, as well as how this compares to the pattern in other
countries or previous studies. This has not been systematically done. Furthermore, some issues regarding the interpretation of results needs to be further developed, as explained in the points below.

Reply

As rightly suggested, the pattern of geographical variation is now described in greater detail, and the possible reasons for such variation discussed. In addition, the precise reason why the difference between El Prat and other studies is so remarkable, is addressed. Moreover, we emphasize the interesting sex- and age-related pattern, and mention some possible causes for this in the Discussion section, empirically supported by European studies on stroke incidence and post-stroke case fatality (page 10).

Comment

4. Authors need to define more clearly in the text as well as in the tables what is meant by suburban. Further discussion on why suburban populations have a higher prevalence of stroke is necessary.

Reply

(a) More information on demographic characteristics has been added. Rural populations had under 2,000 and urban populations over 10,000 inhabitants. Urban, metropolitan populations with high proportion of immigrants were denoted as suburban. An urban mixed category was used to identify former rural populations which had become urban in recent decades through urban sprawl;

(b) As will be seen from the text, we feel that differences in prevalence might be explained by stroke in immigrant populations with highest risk, acquired in their places of origin. In view of the fact that the El Prat survey was the most recently conducted, that screening was performed by a neurologist, and that a considerable part of the immigrant population came from Andalusia and Extremadura -both being southern Spanish regions where stroke mortality has been reported to be highest- we are inclined to speculate that these high figures might in part be explained by high stroke ascertainment in a population at high risk for stroke.

General remarks:

Comment

5. Authors claim that there is three-fold variation in the prevalence of stroke in Spain. However, a careful analysis of the tables shows that the prevalence of stroke is relatively similar across several Spanish populations, with El Prat de Llobregat being the clearest exception, as prevalence rates are considerably higher in this population. I
suggest authors comment on these similarities in the interpretation of results, and try to identify the possible causes (further to higher precision in measurement), which could explain both similarities and differences.

Reply

We quite agree (viz., "A remarkable characteristic of the geographical variation in prevalence in Spanish populations are the high discordant figures registered for El Prat, with most of the remaining values lying in the medium to low ranges," ) and an explanation has now been added, as suggested.

Comment

6. Further to point 4, the paper could benefit considerably from further considering the possible causes of the pattern in Spain, particularly regarding the risk factor distribution across the populations involved. As prevalence is a combination of incidence and case-fatality, it would be good to comment on the potential pathways in regard to these two outcomes, which could explain the pattern.

Reply

This point is similar to point 3. More information on geographical variation has been added, including the remarkable difference between El Prat and other studies, the sex- and age-pattern-related text and comments have been redrafted, and data have been added to Table 1 with regard to study characteristics.

Comment

7. Differences between men and women in the age-patterning of stroke prevalence is probably due to a generalized pattern of women developing stroke at later ages than men. Furthermore, authors comment that the higher proportion of women than men might reflect a better survival prospect among the former. However, this is simply a generalized pattern observed even for the general population (higher proportion of women than men), and it is simply related to higher life expectancy among women than men. I suggest authors re-interpret these patterns.

8. The prevalence of stroke seemed to decrease at very old ages. This is likely to be due to selective survival (also called mortality selection). I suggest authors comment on the potential role of this explanation.

Reply

A new paragraph has been added addressing age- and sex-patterns. Important age- and sex-related characteristics of stroke prevalence, such as the fall in prevalence among elderly men, the rising trend among women, and the high percentage of women in the elderly stroke population, are shared by the Spanish and remaining European
populations. These traits may characterise stroke in Europe and highlight the relevance of gender in the care of elderly stroke patients, possibly suggesting: 1) that women develop stroke at a later age than do men, as observed in Spanish studies; 2) that male stroke sufferers have worse survival prospects than do their female counterparts; and 3) that such sex-selective survival is particularly evident at very old ages.

Comment
9. The way authors describe percentages and refer to significant differences in the text is confusing and can be improved. For instance, authors state in the abstract Prevalence was significantly, 21%, lower in women OR 0.79 95% CI 0.68–0.93. It is not clear what the 21% is referring to (probably the odds ratio difference indication). Please re-write these texts so that the paper reads more smoothly all throughout.

Reply
As suggested, the text has been re-written. Prevalence was significantly lower in women, OR 0.79 95% CI 0.68–0.93, increased with age and displayed a threefold spatial variation with statistically significant differences. Prevalence were highest, 8.7%, in suburban, and lowest, 3.8%, in rural populations. Compared to pooled Spanish populations, statistically significant differences of prevalence, were seen in eight Italian populations, OR 1.39 and Kungsholmen, Sweden, OR 0.40, respectively.