Reviewer’s report

Title: Stroke in urban and rural populations in north-east Bulgaria: incidence and case fatality findings from a 'hot pursuit' study

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Reviewer: Dr Thomas Truelsen

Level of interest: A paper of considerable general medical or scientific interest

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

The study is a "hot pursuit" stroke study on the incidence of stroke and 28 day case fatality in stroke patients from rural and urban areas in north-east Bulgaria. The authors have sought to follow the criteria for a "ideal" stroke study and a total of 351 first-time ever stroke were identified. In women the rural stroke incidence rates were approximately double the urban rates, and in men the rural stroke incidence rates were 1.5 times higher than in the urban population. There is a general lack of good stroke studies from East European countries and it is therefore of importance to get more data on stroke occurrence and case fatality from populations in these countries.

Discretionary revisions:

1. The criteria for external comparisons published by Sudlow and Warlow were largely based on the criteria published by Malmgren R et al (Lancet. 1987;2:1196-1200). Most of the comparisons in the present paper are based on data from the Sudlow et al papers but I suggest that the original publication on "ideal" stroke criteria at least is included as a reference.

2. The authors write p.10 that the incidence rates were slightly higher in November to April, this should be tested statistically.

3. On p.11 the authors write that the CF was related non-linearly to age: it was 35% overall, 30% in

Compulsory revisions:

1. There is little literature on the validity of using verbal autopsy for stroke as a cause of death in adults, but a few validations studies have been done (for example by Chandramohan et al.). Did the authors in the present study use predefined algorithms or was a diagnosis of stroke based only on the interview? A basic discussion of the use of verbal autopsy is missing in Discussion.
2. In Methods it is stated that confidence intervals for standardised rates and for ratios were calculated by standard methods and then there is a reference to a textbook on epidemiology. This is insufficient - the authors must provide at least a name or a more specific reference for the statistical method. In Table 2 it is stated that the Poisson distribution was used for calculating - should also be in Methods.

3. The second paragraph in Results p.9 needs revision as many of the results are repetitions of the ones given in the first paragraph.

4. The proportion of subtypes may not be representative for the entire population as this information was available for only 129 of the 351 stroke patients. It is written on p.10 that the higher proportion of hemorrhagic events are due to selection biases of unknown magnitude. Although the biases may be of unknown magnitude there are several likely biases that should be discussed: patients with known subtype are likely to differ from patients with unknown type on for example average age, sex, urban/rural location.

5. Figure 2 is potentially interesting, but hard to follow. It is the rate ratios that are shown but what is (are) the reference rate(s)?

6. The last sentence in paragraph one on p.11 needs rewriting. It is not easy to follow what the authors mean when they say that "Differences between Varna and western populations in age-standardised rates thus underestimate the differences in healthy life lost because of stroke". Are the authors referring to the weighting used for standard rates? The healthy life years lost due to a disease are calculated in for example the global burden of disease study but includes a measure of the disability rate which is not included in the present paper. Alternatively the authors may refer to the years of life lost due to stroke as compared to a reference population (YLLs).

7. I suggest that the results for CF and severity are presented in a table by sex and age. It is important data and it is hard to extract the results in the current form. I think the reader should have an opportunity to see how different the rates are between rural and urban regions. I am not convinced that under-ascertainment can be completely ignored as a possibility given the present data. These results should be given more emphasis than for example Figure 2 where the results easily could be reported in the text.

8. The Discussion needs substantial expansion. The results should be discussed with results from other stroke studies in East European countries for example Lithuania, Poland, and the former East Germany. There is available literature that has been published in leading stroke journals. Also, the differences in rates between rural and urban populations should be discussed with reference to other studies that also have results from two such populations.

9. The Discussion also needs expansion with regards to possible explanations for the differences in stroke rates between urban and rural populations. In Background the authors refer to the existence of data on smoking prevalence and blood pressure, and although they may not provide a consistent answer why the stroke rates differ it should be further discussed with reference to the present study. What about the access to anti-hypertensive treatment in urban and rural areas? Is diabetes a (known) problem? What about dietary differences (for example reference to: BMJ 1998 Apr 4;316(7137):1047-51)?

**Competing interests:**

None declared.