For attn of Marinette Lacson

Journal Editorial Office
BioMed Central

Dear Ms Lacson,

Thank you for considering our article for publication in BMC Cardiovascular Disorders. According to the main points raised by the reviewers, we made changes to the article (changes marked in Italic) and summarize these in the letter below:

Referee 1:

Question 1)

Why examine only these three counties? The authors stated that these were chosen based on significant differences in changes in mortality, does that mean then that the other counties had no changes? Wouldn’t including all counties have provided more power? Even if the mortality rates didn’t change then you would expect that anti-hypertensive use had not changed either. By choosing only these three the sample appears biased. How does these counties compare with the country as a whole.

Answer to question 1)

Following a preliminary analysis of stroke mortality changes per 100 000 inhabitants in different counties, three counties were selected: Baranya, Bekes and Hajdu-Bihar based on the significant differences in the change in mortality due to stroke.

Of the 19 counties in Hungary Hajdu-Bihar had the lowest stroke mortality in the two years: 132.3/100 000 inhabitants in 2003 and 83.2/100 000 inhabitants in 2008. Bekes showed the 2nd highest mortality (200.5/100 000 inhabitants) in
2008 but compared to the first highest (Zala county with 212.4/100 000 inhabitants) showed less improvement (36.5 versus 57.4) during the 6 years of examination. Baranya had the 3rd lowest stroke mortality rate (124.8/100 000 inhabitants) in 2008 (without considering Hajdu-Bihar which was already included), but started from a higher level (173.5/100 000 inhabitants) in 2003, so the improvement was higher (48.7) in this county than in Pest county (32.1) and the capital Budapest (43.7). So we ended up with three counties: one (Hajdu-Bihar) with the lowest stroke mortality rates in 2003 and 2008, another (Bekes) with the lowest improvement among the counties with high mortality rate in 2008, and one (Baranya) with the best improvement among the ones with lowest mortality rate in 2008. In order to find out differences in the anti-hypertensive treatment, and possible association with the stroke mortality changes, we analyzed these three counties with different specific patterns of change in stroke mortality.

Question 2)

Much more description of the analyses is needed and should be reflected in the results.

Answer to question 2)

The relationship between standardized yearly rates of mortality per 100 000 inhabitants in each county and the yearly days of treatment per each therapeutic group corrected to the county population was examined. This analysis was designed to assess the association between the changes in prescriptions and the changes in mortality rates as a function of time (years). We also determined the correlation coefficients between the number of days of treatment and mortality rates (Table 3 included with all correlations analyzed). All of the computations were solved using MedCalc and Zaitun Times Series statistical softwares. The applied statistical methods were: Normality test, time series analyses, correlation coefficient, paired samples test, one sample test and chi-square test.

Question 3)

Are there other changes in the population or healthcare system that might also have impacted mortality rates. These potential confounders should be addressed.

Answer to question 3)

Stroke-mortality is influenced by many factors and the data presented here are intended mainly to raise awareness to some of them. Life-style parameters/measurements and treatments of risk factors other than hypertension were not included, The overall cardiovascular risk factors of the Hungarian population are likely to have increased (obesity, diabetes mellitus), while leisure-time physical activity and smoking data did not change over the studied time frame. The lack of breakdown of these data on a county level made the authors include association with antihypertensive treatments only, as the main influencing factor in stroke mortality. Improvement of the acute care of stroke
patients could also have a positive influence on mortality rates. In the future a wider analysis of influencing factors could lead to more precise statements about causes of the differences experienced amongst counties.

Question 4)
It is important not to overstate the results, at most all that can be said is that there is an association, not necessarily causal, between medication use and stroke mortality rates.

Answer to question 4)
Considering the other influencing factors not included in this study we have corrected the overstated expressions and used wording of “association”, “correlation” between the findings regarding mortality rate and antihypertensive treatment.

Referee 2:
In addition, statistical methods should be more clearly detailed and the prognostic impact of different blood pressure lowering regimens was not formally investigated.

Answer to Referee 2:
We have added more details to the description of the statistical analysis and added the table 3 containing correlation and significance data for all groups of treatments and pairs of counties.

We have uploaded the changes on the site.

Hope the answers provide enough details to fulfill expectations of the Editorial Board.
Looking forward to a positive decision,

Kind regards,
Albert Császár