Author's response to reviews

Title: Age of onset in chronic diseases: New methods and application to dementia in Germany

Authors:

Ralph Brinks (ralph.brinks@ddz.uni-duesseldorf.de)
Sandra Landwehr (sandra.landwehr@ddz.uni-duesseldorf.de)
Regina Waldeyer (regina.waldeyer@ddz.uni-duesseldorf.de)

Version: 3 Date: 9 April 2013

Author's response to reviews: see over
Reviewer's report:
The authors develop a new method to assess the age of onset of dementia in Germany. The authors have submitted a much improved revision of their manuscript, which was already very strong. The paper makes many contributions and I strongly encourage the authors to edit the text a bit to highlight these contributions.

Major Compulsory Revisions
1. Abstract. The background sentences aren't really that compelling. I think there are two relevant points to the background. First, tell me why dementia is an especially burdensome chronic disease in Germany (years of life lost? cost? prevalence?)? Second, tell me why knowing the age of onset is important. Why is age of onset a better alternative to disease patterns than say incidence?
   We made these two points clearer by revising the whole paragraph. The age of onset (AoO) is an important characteristic, but is not “better” than the incidence. As the formulas in the article show, calculation of AoO uses incidence as an ingredient.

2. Abstract. I think more conversational language would be fine. For example, "We develop an incidence-prevalence-mortality model to estimate the mean and variance of the age of onset in chronic diseases."
   We did as the reviewer suggested, thank you.

3. Background. I think Introduction might be a more appropriate name for this section and fit with other PHM papers.
   OK.
   First paragraph--I’d like to see this exclusively German focused. The paper is about German dementia, not global dementia. I like this paragraph--it sets the stage of what we know and why we should care. But I want to know why I should care about Germany and dementia.
   Germany is the country with most inhabitants in Europe. We added some additional points why Germany is important.
   Second paragraph--what don’t we know? What is the research gap? Why is the age of onset a more appealing measure of burden than incidence? I think this is a key point. Can I reach the wrong conclusion about the burden of dementia by looking at other indicators that I wouldn’t reach by looking at the age of onset? Third paragraph--how does this paper help to solve what we don’t know. How does this paper help to fill the research gap. I had to find the answer to this question buried in the paper. Instead, highlight the contribution of this paper. The authors have identified a better measure (still need to convince readers that age of onset is better) and also develop a method to measure age of onset. That’s their contribution, as I understand the paper.
   We added a description about the research gap (AoO of dementia is not easily accessible), and how we fill the gap (calculating AoO by our formulas). The authors do not think that AoO is a better measure than incidence. We think it is an important measure. However, it has to be interpreted with care, because it depends on the age distribution of the population. We added this point.

4. I’m still not sure why R is not R(a). Maybe m1(a) / m0(a) is 2.4 for all ages a? I can imagine many readers will be confused about this point.
   We agree with the reviewer. However, the age-specific values are not reported. We added an additional explanation about this point and mentioned this point later in the discussion (weaknesses of the work).

5. I agree with my fellow reviewer. If the authors are able to make their R code available as a technical appendix, that would increase citations to the paper.
   As both reviewers suggested this point, we created a zip-file which contains 1) the source files, 2) the age pyramids for Germany in 2002 and 3) a readme file with all instructions to get the script running under R.
6. Discussion. The 2nd and 3rd sentences are key points of this paper. The age distribution is the reason why age of onset might be a better indicator than other measures. I would like to see this point in the introduction because it's counter-intuitive and brings the reader into the paper. We added these points in the introduction.

7. Discussion. The research gap and contribution are buried in the discussion and should be highlighted in the introduction. "Finally the approach presented in this article for the first time...". That's the contribution of this paper. "Currently there are no patient registers...". That's part of the research gap. The research gap and our solution are now mentioned in the introduction.

Minor Essential Revisions
1. Abstract. Why 2002? Is there more recent data available? There is some data from 2010, but it is far less valuable. The 2010 data are from a single health insurance, and we think it is selection-biased (the insurance is known for that).

2. Remove so-called in Methods. We did so, thank you.

3. Change verb from "get" to "obtain" on page 4. Done.

4. Move reference to Figure 1 at the end of sentence and in parentheses on page 4. OK, we did so, thanks.

5. I find the order of terms confusing on page 4. Start with $N=S+C$, then $p=C/N$. So $S=(1-p)N$. OK.

6. Label the y-axes of the figures. And maybe las=1 to turn the text horizontal? The y-axes are labeled now. Most of PHM graphs have vertical texts on the ordinate.