Reviewer's report

Title: Forecasts of COPD mortality in Australia: 2006-2025

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Reviewer: Annunziata Faustini

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COMMENTS TO AUTHORS

The authors estimated the COPD mortality trends in Australia, separately for men and women. After reconstructing the mortality rates (Australia, 1922-2005, in 50-year-olds) in 5-year age groups and by gender, they applied functional time-series models to the data to estimate the functional relationship between age and COPD mortality. They then used these functions to forecast mortality rates for males and females in two next decades. Mortality decreased over time, between 1922 and 1950 especially for 75+year-old among both males and females; it reached the lowest values in the 1950s. The subsequent mortality rate trends, though increasing in both males and females, differed. Men under 80 years of age presented a first peak in 1970 and a second peak in the 80s; afterwards, rates declined in all age groups until 2006. Mortality rates in women increased, but started later (from 1960s) than it was for men, and had similar trends in all age groups, reaching peaks in the 1990s and decreasing slowly afterwards. The forecast trends clearly decreased in all age groups in males, but only in some age groups in females.

MAJOR GENERAL COMMENTS

The paper deals with a current and interesting problem, i.e. to predict the burden of chronic diseases, especially COPD. The authors presented a new statistical approach to forecast COPD mortality and discussed exhaustively the strengths and limits of this approach.

I have a few general observations: 1) First of all, prevalence is the best indicator, in the case of COPD, to analyze the disease burden and to program health interventions. Mortality, rather, is a general population health indicator, but it may be very useful in assessing the treatment outcomes in specific cohorts of patients. As was suggested by the WHO for TB and it was done in the Netherlands for COPD, mortality analysed together with prevalence and incidence of a disease may also help health programmes to assess priorities of disease prevention or disease management.

2) The statistical approach the authors adopted here has been less used and generally, to compare mortality among patients with a specific disease in different countries, thus to give an assessment of its performance it should be compared with more traditional methods to predict health events. 3) Although the authors gave an exhaustive review of the limits, it appears as a formal list; e.g. smoking is the most important risk factor in developing COPD not in dying from COPD;
however the latency period from smoking to disease appearance has not been defined and the cohort effect could take a long time. In contrast, they only mention the possibility of new treatment able to prolong the lives of COPD patients, but the beta2-agonists have been used since the early 1970s and Australia is the country where thiotropium was first registered, although more recently.

MINOR ESSENTIAL REVISION

• The authors used a very long period to estimate COPD rates starting from 1920s; this is generally useful to stabilize the trend. In this case however, as the authors themselves stated, the estimates up to the 1950s vary greatly, especially among females and the oldest people; the important decrease in the same period is very poorly explained and many factors could have influenced the trend, including factors that make the two periods (before and after the 1950s) incomparable such as COPD diagnosis, disease ICD-9 codes, and the possible impact of the two world wars. I suggest the authors carry out a sensitivity analysis excluding data before 1960.

• Another reason for this alternative analysis is not having took into account cohort effect in the models. Now, although the authors declared their only assumption to be that mortality increased monotonically with age, other not so explicit assumptions were made in forecasting future estimates, such as that relationship between age and mortality is stable over time and no factors changed this relationship in COPD patients. I read an interesting article by the first author concluding that these models may be applied to predict future trends of diseases for which advancements in treatment were very rare and cohort effects were minimal. I absolutely agree with this conclusion; but this implies that efficacious treatments in models will be included or additional survival time the treatments add will be taken into account.

DISCRETIONARY REVISION

- Methods to forecast data have to be briefly reported in the paper; only referring to a previous paper is not enough.
- In the abstract the results for females are not coherent with the forecast trend in figure n.4.
- Reference 20 is incorrectly reported on page 13, since it does not refer to an Australian study.
- The authors reported the ICD-10 codes that were introduced in the mid 2000s.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare that I have no competing interests