PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Variability in the burden of disease estimates with or without age weighting and discounting: a methodological study
AUTHORS	Egunsola, Oluwaseun; Raubenheimer, Jacques; Buckley, Nicholas

VERSION 1 – REVIEW

REVIEWER	Peng Minjin Department of Infection Control, Taihe Hospital, Hubei University of Medicine, Shiyan 442000, China
REVIEW RETURNED	17-Jan-2019

GENERAL COMMENTS	Thanks for the review inviting. This study is a confirmatory discussion on YLL and YPLL for the estimation of the burden of disease. The article was well written and revelatory for healthcare policy and research. However, there were several suggestions for this article in my personal opinion. 1. The references up-to-date need to be reviewed and supplied. 2.In page 4 line 42-49 'Methods of YPLL…… all the ages', YPLL need to be explained in detail. 3. In page 6 line 27-28 'YLL with non-uniform age weighting: YLL (nuWT & Disc)', maybe means 'YLL with non-uniform age weighting and discounting: YLL (nuWT & Disc)'? 4.In the results part, examples were data interpretation of Australia and the USA, were there difference among the three countries? May Data interpretation of South Africa be more appealing? 5. In page 8 line 14-18 'YPLL estimates ……opposite bias'. In my opinion, the higher estimates of YPLL was compared with YLL, the explanation 'with YLL demonstrating opposite bias ' was not appropriate. 6. In page 10 line 18-23 'the decision as to whether a year of life gained now is worth more than one gained in 10 years will depend on societal perceptions of life, which can be very heterogeneous, especially in highly multicultural societies.' could be rewritten with words easier to understand.

REVIEWER	Brecht Devleesschauwer Sciensano, Belgium
REVIEW RETURNED	27-Feb-2019

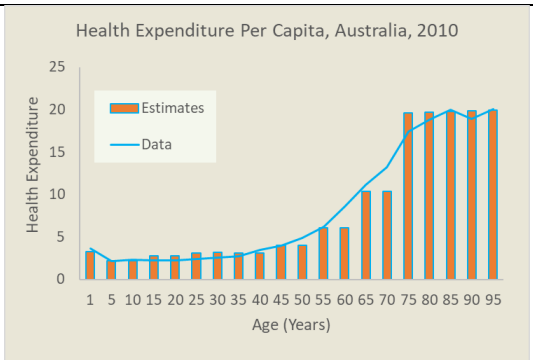
GENERAL COMMENTS	The authors explore different methods for calculating burden of disease due to fatal health outcomes. While technically correct, the manuscript remains somewhat superficial and does not provide novel insights. Indeed comparisons of different approaches for calculating burden of disease (age weighting, time discounting, reference life expectancy) have been performed before. The current manuscript also fails to integrate the current methods of the GBD study -- the most recent reference dates from 2009. Some specific points: * Please use line numbers. ABSTRACT * "mortality data was" -> "mortality data were" * "World Health Organisation" -> "World Health Organization" (also in Methods) * Please specify how "total national burden of disease" was obtained and defined. * The Results part does not talk about the effects of discounting INTRODUCTION * "have differed slightly": what exactly were the differences? Choosing different max age can have a big impact, eg 65 vs 75, and the choice remains arbitrary.. * ".. time-based discounting and age weighting are not incorporated into YPLL calculations. For YLL however, time-based discounting and age weighting may be incorporated.": this is misleading, because time discounting and age weighting may also be incorporated in YPLL. It would therefore be much more useful to compare the effect of the three varying elements separately, ie, choice of reference life expectancy, use of time discounting, use of age weighting. * "The GBD study for example, utilised a discount rate of 3%": please specify which GBD study you are referring to, because time discounting and age weighting are no longer used since the GBD 2010 study. Having a more recent view of literature would thus be most welcome. * No background information is provided on age weighting METHODS * "..but before age of life expectancy" -> please specify that this is "life expectancy at birth" * Please describe the age weighting function you applied. * Please describe which standard life expectancy table was used. * "the standard life expectancies for the average ages of deaths": please describe how average age of death was calculated -- as the mean of the lower and upper bound of the age group?

	* "Four metrics were compared": please refer to existing literature for a more standardized way of labeling the different options, eg, YLL[1; 0.03] for YLLs with age weighting and 3% discount rate. * "..for a given age group by the expected life at the mid-point..."; expected life expectancy? * Why was a cut-point of 79 used? * The YPLL formula is incorrect, as it can lead to negative values * "total national burden of disease": how was this defined/obtained/calculated? RESULTS * There is nothing on the effect of discounting? * The higher contribution of causes of death among younger adults, when calculating YPLL, is somewhat contradictory: for each individual death, the contribution will be smaller compared to (no frills) YLLs. However, because the contribution of deaths in older age groups is even further reduced, the *relative* contribution of the causes in younger adults is increased. DISCUSSION * "YPLL estimates were relatively higher"; but smaller in absolute terms! * The statements on funding are somewhat naive: first of all, there are many good reasons why funding priorities should not have a one to one relationship with burden of disease, because funding depends on many other factors. Second, the funding of infectious disease research and control is highly relevant to keep the burden low -- low burden does not mean not dangerous! * resources on their website: please provide URL * "Although the WHO has shown a preference for time-based discounting with age weighting"; this statement is based on a document published in 2003, which is 16 years ago. The authors would benefit from getting a more recent view of literature and WHO burden of disease studies. * "deaths beyond the life expectancy" -> "life expectancy at birth" CONCLUSION * "Given the variability in the estimates of the burden of disease with different approaches, the burden of disease should not be the only criterion for prioritizing health or research funding.": this is anyhow not the case, but not because there is variability in estimates. Every aspect of decision making will be prone to methodological uncertainty -- does this mean we cannot use any of those aspects? * "Different metrics should be considered before resources are allocated.": this does not solve the problem and just makes it more

	difficult to make decisions; What is more important is to have transparency about methods, and to use methods that correspond to the societal values that are held by stakeholders and/or general public

REVIEWER	Christos H Skiadas ManLab, Technical University of Crete, Greece
REVIEW RETURNED	04-Mar-2019

GENERAL COMMENTS	Years of life lost or years of potential life lost: Implications for the estimation of the burden of disease Oluwaseun Egunsola, Jacques Raubenheimer, Nicholas Buckley The Authors of this study use some classical and well established methods and techniques to calculate the years of life list or the years of potential life lost. They use these estimates to examine the impact on these methods on the estimation of the burden of diseases. In their Conclusions argue that “Given the variability in the estimates of the burden of disease with different approaches, a single measure of the burden of disease should not be the only criterion for prioritizing health or research funding”. Clearly the research emerged more questions and emphasized the need for standardizing the approved lines for the “health priorities”. To my view the strong part of the study had to do with some important points raised as is the need for an accepted “metrics system” of disease burden and the need or not of a priority in relative research funding given the variability in the estimates of the burden of disease. However, it must be noted that the burden of disease studies passed from several reformulations and adaptations in the last 30 years until the forms accepted in nowadays. As a very “heavy” international system needs a data collection standardization that is always in progress following the new computer facilities and skilled data sets collectors along with well-educated data analysis and statistics staff. The paper in view provides hints to help improving the burden of decease system by taking into account some of the points raised than to totally reformulate the methodology used. To this end the authors include their task in the title by adding clearly “Implications for the estimation of the burden of disease.” Furthermore, the questions raised regarding a health resource allocation system faces the emerging need for health expenditure data availability. In the majority of cases health expenditure data are provided as a percentage of the total country income or as a simple number of total expenditure in a country or per capita. Only few countries provide data allocated per age group or per disease and age group. It is like to face a barrier between researchers working in the burden of disease group and the people scheduling the health expenditure programs and more with those making the governmental decisions. The authors could check if the health expenditure data per age group in Australia (see figure from our application) and in USA could help them to check the methodologies and results obtained at least for the total decease age group. I have no information for South Africa data availability.

	 Public spending on health and long-term care: a new set of projections - © OECD 2013 Few special details for the paper: The selection of the life expectancy as a bar in graphs is of course reasonable to appear. However, looking further to the graphs it looks like another bar at the “maximum death rate” or “mode” location will be proven interesting. Some of the core diseases tend to peak around this important point. Similar point exists for the health expenditure as well. Graphs: Too many cases in the same graph. It could be more interesting to present “important cases” separately. Some of the many details with numbers and percentages could be included inside the text in Tables. Bibliography: There are adequate references Concluding, I suggest this paper for publication under minor changes.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1

1. The references up-to-date need to be reviewed and supplied.

We have included more recent references where possible.

2. In page 4 line 42-49 ‘Methods of YPLL…… all the ages’, YPLL need to be explained in detail.

We have provided a more detailed explanation on page 4 of the introduction.

3. In page 6 line 27-28 ‘YLL with non-uniform age weighting: YLL (nuWT & Disc)’, maybe means ‘YLL with non-uniform age weighting and discounting: YLL (nuWT & Disc)’?

Thank you. We have corrected this.

4. In the results part, examples were data interpretation of Australia and the USA, were there difference among the three countries? May Data interpretation of South Africa be more appealing?

We have included results for South Africa on pages 8 and 9 of the results and also referenced figure 4.

5. In page 8 line 14-18 ‘YPLL estimates ……opposite bias’. In my opinion, the higher estimates of YPLL was compared with YLL, the explanation ‘with YLL demonstrating opposite bias ’ was not appropriate.

We have modified this sentence on page 10 of the discussion.

6. In page 10 line 18-23 ‘the decision as to whether a year of life gained now is worth more than one gained in 10 years will depend on societal perceptions of life, which can be very heterogeneous, especially in highly multicultural societies.’ Could be rewritten with words easier to understand.

We have re-written this sentence on page 12 of the discussion

Reviewer 2

ABSTRACT

1. "mortality data was" -> "mortality data were"

We have corrected this

2. "World Health Organisation" -> "World Health Organization" (also in Methods)

We have corrected this

3. Please specify how "total national burden of disease" was obtained and defined.

We have specified this on page 7 of the methods

4. The Results part does not talk about the effects of discounting

Previously, only a single standard life table was used to estimate YLL for the three countries. We have changed this methodology and have now used the 2014 life tables for each country. We have included the results for discounting with or without age weighting on pages 8 and 9 of the results.

INTRODUCTION

5. "have differed slightly": what exactly were the differences? Choosing different max age can have a big impact, eg 65 vs 75, and the choice remains arbitrary.

We have modified this sentence on page 4 of the introduction.

6. ".. time-based discounting and age weighting are not incorporated into YPLL calculations. For YLL however, time-based discounting and age weighting may be incorporated.": this is misleading, because time discounting and age weighting may also be incorporated in YPLL. It would therefore be much more useful to compare the effect of the three varying elements separately, ie, choice of reference life expectancy, use of time discounting, use of age weighting.

We have modified this statement on page 4 of the introduction

7. "The GBD study for example, utilised a discount rate of 3%": please specify which GBD study you are referring to, because time discounting and age weighting are no longer used since the GBD 2010 study. Having a more recent view of literature would thus be most welcome.

We have modified this sentence on page 5 of the introduction.

8. No background information is provided on age weighting

We have included background information on age weighting on page 5

METHODS

9. "..but before age of life expectancy" -> please specify that this is "life expectancy at birth"

We have specified this

10. Please describe the age weighting function you applied.

We have described this on pages 6 and 7

11. Please describe which standard life expectancy table was used.

We have included a sentence on the source of the life tables used on page 7 and included a reference 13.

12. "the standard life expectancies for the average ages of deaths": please describe how average age of death was calculated -- as the mean of the lower and upper bound of the age group?

We have included the method of calculation on page 6

13. "Four metrics were compared": please refer to existing literature for a more standardized way of labeling the different options, eg, YLL[1; 0.03] for YLLs with age weighting and 3% discount rate.

We have made the suggested changes

14. "..for a given age group by the expected life at the mid-point.."; expected life expectancy?

We have corrected this sentence

15. Why was a cut-point of 79 used?

We used the Australian Bureau of statistics cut-off value.

16. The YPLL formula is incorrect, as it can lead to negative values

We used the YPLL formula as provided on the Australian Bureau of statistics website.(1) Since our aim is to compare existing methods used in practise, we cannot change this.

17. "total national burden of disease": how was this defined/obtained/calculated?

We have included this in the methods on page 7

RESULTS

18. There is nothing on the effect of discounting?

We have added results of discounting on pages 8 and 9

19. The higher contribution of causes of death among younger adults, when calculating YPLL, is somewhat contradictory: for each individual death, the contribution will be smaller compared to (no frills) YLLs. However, because the contribution of deaths in older age groups is even further reduced, the *relative* contribution of the causes in younger adults is increased.

We have added a sentence about this in the discussion on page 10

DISCUSSION

20. "YPLL estimates were relatively higher"; but smaller in absolute terms!

We have amended this sentence.

21. The statements on funding are somewhat naive: first of all, there are many good reasons why funding priorities should not have a one to one relationship with burden of disease, because funding depends on many other factors. Second, the funding of infectious disease research and control is highly relevant to keep the burden low -- low burden does not mean not dangerous!

We do realise that the burden of disease is not the sole criterion for funding priorities. We have modified this section of the discussion.

22. resources on their website: please provide URL

We have provided a reference for this

23. "Although the WHO has shown a preference for time-based discounting with age weighting"; this statement is based on a document published in 2003, which is 16 years ago. The authors would benefit from getting a more recent view of literature and WHO burden of disease studies.

We have amended this on page 11

24. "deaths beyond the life expectancy" -> "life expectancy at birth"

We have amended the statement on page 12

CONCLUSION

25. "Given the variability in the estimates of the burden of disease with different approaches, the burden of disease should not be the only criterion for prioritizing health or research funding.": this is anyhow not the case, but not because there is variability in estimates. Every aspect of decision making will be prone to methodological uncertainty -- does this mean we cannot use any of those aspects?

We have amended the concluding statements

26. "Different metrics should be considered before resources are allocated.": this does not solve the problem and just makes it more difficult to make decisions; What is more important is to have transparency about methods, and to use methods that correspond to the societal values that are held by stakeholders and/or general public

We have amended the concluding statements

Reviewer 3

The Authors of this study use some classical and well established methods and techniques to calculate the years of life list or the years of potential life lost. They use these estimates to examine the impact on these methods on the estimation of the burden of diseases.

In their Conclusions argue that “Given the variability in the estimates of the burden of disease with different approaches, a single measure of the burden of disease should not be the only criterion for prioritizing health or research funding”.

Clearly the research emerged more questions and emphasized the need for standardizing the approved lines for the “health priorities”. To my view the strong part of the study had to do with some

important points raised as is the need for an accepted “metrics system” of disease burden and the need or not of a priority in relative research funding given the variability in the estimates of the burden of disease. However, it must be noted that the burden of disease studies passed from several reformulations and adaptations in the last 30 years until the forms accepted in nowadays. As a very “heavy” international system needs a data collection standardization that is always in progress following the new computer facilities and skilled data sets collectors along with well-educated data analysis and statistics staff. The paper in view provides hints to help improving the burden of decease system by taking into account some of the points raised than to totally reformulate the methodology used. To this end the authors include their task in the title by adding clearly “Implications for the estimation of the burden of disease.”
Furthermore, the questions raised regarding a health resource allocation system faces the emerging need for health expenditure data availability. In the majority of cases health expenditure data are provided as a percentage of the total country income or as a simple number of total expenditure in a country or per capita. Only few countries provide data allocated per age group or per disease and age group. It is like to face a barrier between researchers working in the burden of disease group and the people scheduling the health expenditure programs and more with those making the governmental decisions.
The authors could check if the health expenditure data per age group in Australia (see figure from our application) and in USA could help them to check the methodologies and results obtained at least for the total decease age group. I have no information for South Africa data availability.
Thank you for the positive comments. Although the suggestion regarding the relationship between health expenditure and methods of estimation of disease burden is relevant, it is however beyond the scope of this present study.

VERSION 2 – REVIEW

REVIEWER	Brecht Devleesschauwer Sciensano, Belgium
REVIEW RETURNED	11-Apr-2019

GENERAL COMMENTS	All comments have been adequately addressed. Two minor editorial things that can be addressed in the final stage: * Please be consistent in the use of YLL() vs YLL[]; I would recommend to use square brackets throughout * Please add the definition of YLL[K;r] in the figure legends

VERSION 2 – AUTHOR RESPONSE

Reviewer 2

1. Please be consistent in the use of YLL() vs YLL[]; I would recommend to use square brackets throughout

We have made the suggested changes.

Please add the definition of YLL[K;r] in the figure legends

We have included these definitions in the figure legend