PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Trends and socioeconomic disparities in all-cause mortality among adults with diagnosed diabetes by race/ethnicity: a population-based cohort study — United States, 1997-2015
AUTHORS	Mercado, Carla; Beckles, Gloria; Cheng, Yiling; Bullard, Kai; Sayday, Sharon; Gregg, Edward; Imperatore, Giuseppina

VERSION 1 – REVIEW

REVIEWER	Peter M Nilsson Lund University, Sweden
REVIEW RETURNED	05-Oct-2020

GENERAL COMMENTS	This was a very relevant and large-scale analysis of trends in all-cause mortality from population surveys 1997 to 2011 (with mortality follow-up until end of 2015) associated with diabetes in the US population, applying an intersectional model when social factors, ethnicity and disease are all taken into account. The statistical analyses are sophisticated why I have recommended that an expert in statistics should be invited to review. Comments: 1. Diabetes should not only be regarded as a (self-reported) diagnosis but also the degree and quality of treatment control. If data are not available on this (HbA1c) or the drug treatment profile this has to be acknowledged 2. Of great importance is to analyse competing mortality risks, but here only total (all-cause) mortality is used. Why not cause-specific mortality, or is that part spared for another manuscript? 3. In Sweden, national data on mortality trends in diabetes and relation to risk factor control have been published, of great relevance to compare for trends and discussing the remaining gaps compared to non-diabetic population. These two papers could be cited as they are from N Engl J Med (Rawshani A, Rawshani A, et al. Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med. 2018 Aug 16;379(7):633-644; and Rawshani A, et al. Mortality and Cardiovascular Disease in Type 1 and Type 2 Diabetes. N Engl J Med. 2017 Apr 13;376(15):1407-1418) 4. Intersectional analyses are often used to analyse the effect of gender in relation to social factors and ethnicity. Why was this approach not applied in the present study? 5. Most importantly, what is the public health message of this study? People in more adverse social conditions seems to have benefited more from the mortality decline, than more affluent people?

REVIEWER	Ryan McGrath

	North Dakota State University
REVIEW RETURNED	24-Oct-2020

GENERAL COMMENTS	BMJOPEN-2020-044158 presents results from the National Health Interview Survey. While some parts of this manuscript were interesting, other areas could be improved. I hope the authors consider my feedback for their manuscript. MAJOR COMMENTS • Introduction: The purpose statement should specify the overall time period observed, and 5-year time period for examining trends. • Outcome: This reviewer understands the data management and analytical procedure; however, the 5-year time period is arguably problematic. Why was a 5-year truncation selected (relative to other time periods), and how could those who experienced mortality beyond this time window have influenced the findings? • Other Covariates: By categorizing other race/ethnicity in the "all" category, the n= in this category will differ from the sum of those identifying as N-H white, N-H black, and Hispanic. You may want to list those identifying as other race and ethnicity as its own category, regardless of lower n=. The presentation of the tables is currently misleading for the "all" category. Otherwise, consider excluding. • Stat Analysis and Results: If the authors are interested in observing changes in trajectories over time it seems unusual to me that change from 1997-2001 to 2007-2011 was examined. The 2002-2006 time period may also provide insights with respect to the research questions. This may have implications for the Discussion. MINOR COMMENTS • Introduction: "…United States from mid-1990s that by 2015 an…" This sentence could be revised for smoother readability. Please consider revision here and where appropriate in the manuscript. • Introduction: In the second paragraph, SEP is defined differently than in the first paragraph. You may want to just consider deleting definitions in an Introduction section. The differing definitions distract the reader. • Data and Population: You may want to clarify that the analytical sample was 380,913, and 8.6% were identified as having diabetes. • Table 1: Can you provide information for mortality here? • Make any changes to the abstract that align with those made in the text. • The referencing of citations was somewhat sloppy. Intext citations were not correctly presented ".(1)" vs. "(1).", and some intext citations were even in superscript (Discussion). My guess is the paper was reformatted in haste with Endnote or similar software.

REVIEWER	Hajime Uno Dana-Farber Cancer Institute
REVIEW RETURNED	22-Nov-2020

GENERAL COMMENTS	The paper investigated the associations of all-cause mortality with various factors. Key variables of interest include diabetes status, year, race/ethnicity, and socioeconomic position. The data from

the National Health Interview Surveys data for 1997-2011 linked with the National Death Index data were used. The authors used the survival information only up to 5 years from the date of the survey interview to reduce follow-up bias. I have some minor comments for possible improvement of the manuscript.

#1. The terminology "5-year mortality rate" is confusing. I am worried that readers may confuse "5-year mortality rate" with the probability of death at Year 5 after the survey interview. The metric the authors calculated is the incidence rate of all-cause mortality based on the data of a 5-year period after the survey interview. I would suggest the authors clarify this and take out "5-year" from the text and tables.

#2. "Age-adjusted" mortality rate.
Please clarify what age distribution in which population the result was adjusted to.

#3. "Weighted Poisson regression" in the statistical analysis section.
Providing some more details about what weights are used would improve the manuscript.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Prof. Peter Nilsson, University of Lund
Comments to the Author:
This was a very relevant and large-scale analysis of trends in all-cause mortality from population surveys 1997 to 2011 (with mortality follow-up until end of 2015) associated with diabetes in the US population, applying an intersectional model when social factors, ethnicity and disease are all taken into account. The statistical analyses are sophisticated why I have recommended that an expert in statistics should be invited to review.
Comments:
1. Diabetes should not only be regarded as a (self-reported) diagnosis but also the degree and quality of treatment control. If data are not available on this (HbA1c) or the drug treatment profile this has to be acknowledged

A sentence was added in the limitations paragraph to address that we were unable to assess diabetes management (regarding quality of care, medication adherence, and HbA1c level) in this study as clinical or physical exam data are not collected in NHIS.

2. Of great importance is to analyse competing mortality risks, but here only total (all-cause) mortality is used. Why not cause-specific mortality, or is that part spared for another manuscript?

It would be wonderful if we could highlight the cause-specific mortality in this study. However, the study design of this project that focused on people with diagnosed diabetes then stratified by race/ethnicity and further by categories of education attainment and income-to-poverty ratio is not designed or sufficiently powered to investigate cause-specific mortality.

3. In Sweden, national data on mortality trends in diabetes and relation to risk factor control have been published, of great relevance to compare for trends and discussing the remaining gaps compared to non-diabetic population. These two papers could be cited as they are from N Engl J Med

(Rawshani A, Rawshani A, et al. Risk Factors, Mortality, and Cardiovascular Outcomes in Patients with Type 2 Diabetes. N Engl J Med. 2018 Aug 16;379(7):633-644; and Rawshani A, et al. Mortality and Cardiovascular Disease in Type 1 and Type 2 Diabetes. N Engl J Med. 2017 Apr 13;376(15):1407-1418)

Thank you for sharing these references. They are insightful. In this study, we evaluated trends in the relationship socioeconomic position and race/ethnicity has on mortality in adults with diabetes in the United States and compared to those without diabetes to see if these changes were experienced as a whole in the US or specific to those with diabetes. These references do not assess socioeconomic status or race/ethnicity and the population is not comparable to the US in the context that socioeconomic status and race/ethnicity has on health and mortality.

4. Intersectional analyses are often used to analyse the effect of gender in relation to social factors and ethnicity. Why was this approach not applied in the present study?

Our original plan was to have separate tables for Women and Men. However, as mentioned on answer for #2 above, the sample size did not allow for further stratification (especially for racial/ethnic minority groups in higher categories of income and education). This limitation is mentioned towards the end of the limitation paragraph. We are planning a future project that can better highlight the effect of gender in relation to social factors and ethnicity.

5. Most importantly, what is the public health message of this study? People in more adverse social conditions seems to have benefited more from the mortality decline, than more affluent people?

The overall take away from this study, as mentioned in the last two sentences of first paragraph on page 15 and in the conclusion section, is that although overall improvements have been observed in mortality over time for all U.S. adults (more so for those with diabetes than without), the socioeconomic (IPR and education) disparity in mortality has remained with no statistical significant change. Basically, the gap in mortality risk between the poorest/less education attainment compared to the richest/highest level of education attainment has not change from 1997-2011 despite the overall decline in mortality rate.

Reviewer: 2
Dr. Ryan McGrath, North Dakota State University Comments to the Author:
BMJOPEN-2020-044158 presents results from the National Health Interview Survey. While some parts of this manuscript were interesting, other areas could be improved. I hope the authors consider my feedback for their manuscript.

MAJOR COMMENTS

• Introduction: The purpose statement should specify the overall time period observed, and 5-year time period for examining trends.

This information was added to the purpose statement in the introduction.

• Outcome: This reviewer understands the data management and analytical procedure; however, the 5-year time period is arguably problematic. Why was a 5-year truncation selected (relative to other time periods), and how could those who experienced mortality beyond this time window have influenced the findings?

Without the 5-year truncation, the mortality rates in the earlier time periods were a lot greater than the 5-year mortality rates due to having a lot more deaths given the much greater follow-up time. The

more recent time periods have limited follow-up time and if considering healthy participant bias, less likely to die within a shorter time frame. To make the year groups (1997-2001, 2002-2006, and 2007-2011) more comparable we limited all to 5-year mortality rates. Otherwise, we have observed a biased greater mortality change from 1997-2001 to 2007-2011.

• Other Covariates: By categorizing other race/ethnicity in the "all" category, the n= in this category will differ from the sum of those identifying as N-H white, N-H black, and Hispanic. You may want to list those identifying as other race and ethnicity as its own category, regardless of lower n=. The presentation of the tables is currently misleading for the "all" category. Otherwise, consider excluding.

This study considered survey design and sample weights to calculate estimates representative of the U.S. population. We have gone back and forth on this issue in that for "all" U.S. population the other race/ethnicity should be included. Due to limited numbers, standalone estimates for this group would be statistically unreliable for this study design. If this group is removed, the category would not be "all" but would be "all minus other race/ethnicity". Nonetheless, the analyses were performed again removing the other race/ethnicity group.

• Stat Analysis and Results: If the authors are interested in observing changes in trajectories over time it seems unusual to me that change from 1997-2001 to 2007-2011 was examined. The 2002-2006 time period may also provide insights with respect to the research questions. This may have implications for the Discussion.

The changes between each time period were added to the tables.

MINOR COMMENTS

• Introduction: "…United States from mid-1990s that by 2015 an…" This sentence could be revised for smoother readability. Please consider revision here and where appropriate in the manuscript.

Sentence was edited.

• Introduction: In the second paragraph, SEP is defined differently than in the first paragraph. You may want to just consider deleting definitions in an Introduction section. The differing definitions distract the reader.

Edited accordingly.

• Data and Population: You may want to clarify that the analytical sample was 380,913, and 8.6% were identified as having diabetes.

We clarified the analytical sample size at the end of the Data and Population section. We did not include the 8.6% because many may want to interpret it as the self-reported diabetes prevalence in the U.S. when in fact it is just the percent of the sample identified as having diabetes (no sample weights or confidence intervals).

• Table 1: Can you provide information for mortality here?

It is unclear what mortality information is being requested.

• Make any changes to the abstract that align with those made in the text.

Edits were made accordingly.

• The referencing of citations was somewhat sloppy. Intext citations were not correctly presented ".(1)" vs. "(1).", and some intext citations were even in superscript (Discussion). My guess is the paper was reformatted in haste with Endnote or similar software.

Thank you for catching this inconsistency. Edits were made throughout.

Reviewer: 3
Dr. Hajime Uno, DF/CHCC
Comments to the Author:
The paper investigated the associations of all-cause mortality with various factors. Key variables of interest include diabetes status, year, race/ethnicity, and socioeconomic position. The data from the National Health Interview Surveys data for 1997-2011 linked with the National Death Index data were used. The authors used the survival information only up to 5 years from the date of the survey interview to reduce follow-up bias. I have some minor comments for possible improvement of the manuscript.

#1. The terminology "5-year mortality rate" is confusing. I am worried that readers may confuse "5-year mortality rate" with the probability of death at Year 5 after the survey interview. The metric the authors calculated is the incidence rate of all-cause mortality based on the data of a 5-year period after the survey interview. I would suggest the authors clarify this and take out "5-year" from the text and tables.

Further clarification was added in "Variables" "Outcome" sub-section of the methods and the label "5-year" was removed throughout.

#2. "Age-adjusted" mortality rate.
Please clarify what age distribution in which population the result was adjusted to.

There was no age standardization as what is being implied by "what age distribution in which population." The mortality rates are age-adjusted in that the variable for participants' baseline age was included in the model when calculating the mortality rate. This is mentioned in the statistical analysis section that the baseline age of the participant was included as a covariate in the model.

#3. "Weighted Poisson regression" in the statistical analysis section. Providing some more details about what weights are used would improve the manuscript.

Although information on sampling weights is included at the end of the first paragraph in Data and Population section, details were added in the second sentence of the Statistical Analysis section.

VERSION 2 – REVIEW

REVIEWER	Peter M Nilsson Lund University, Sweden
REVIEW RETURNED	09-Mar-2021

GENERAL COMMENTS	The manuscript has improved and the authors have explained why some analyses were not possible to do now (i.e. stratification for gender) but might be possible to do in the future.

REVIEWER	Hajime Uno Dana-Farber Cancer Institute
REVIEW RETURNED	14-Mar-2021

GENERAL COMMENTS	The authors addressed all my comments satisfactorily. I do not have any further comments or questions.