PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Sedentary behavior and life expectancy in the United States: A cause-deleted life table analysis
AUTHORS	Peter T. Katzmarzyk and I-Min Lee

VERSION 1 - REVIEW

REVIEWER	David Berrigan and Richard P. Troiano Applied Research Program Division of Cancer Control and Population Sciences National Cancer Institute We have no competing interests to declare
REVIEW RETURNED	27/01/2012

GENERAL COMMENTS	This paper presents calculations of the effect of sedentary time on life expectancy in the US. In light of the high prevalence of sedentary behavior and evidence that sedentary time is associated with poor health and increased mortality, it seems worthwhile to place its effects on a common metric such as years of life lost. While a valuable contribution, the paper could be stronger with the provision of additional information. 1. The calculations are based on self reported prevalence of sitting and television viewing from 2005-2006 and 2007-2008 NHANES, a large health survey in the United States. It is not clear why prevalence based on TV came from 2005-2006 and sitting prevalence came from 2007-2008. 2. Self report has many cognitive challenges as well as potential for recall bias. The authors discuss these issues. However, why not compare the calculations with similar calculations based on objectively measured sedentary time? NHANES 2003-2006 included an accelerometer component and estimates of sedentary time based on these objective measurements have already been published (Matthews et al. 2008). This paper would be much more interesting if it contrasted the estimated effects of sedentary time on life expectancy based on self reported versus objectively measured sedentary time. 3. The estimates of the mortality effects of sedentary time are based on five studies. Recent reviews by Proper et al (2011) and Thorp et al. (2011) come up with different numbers of salient studies. More detail concerning the inclusion/exclusion criteria for this meta-analysis would be helpful.. 4. In the discussion on page 9, the authors note that “assumptions had to be made when estimating the exposure levels in NHANES.” These assumptions should be described in the Methods. 5. Perhaps the analysis could be illustrated by a figure of some kind. Such a figure might serve highlight some of the assumptions of the cause deleted life table approach as implemented here. In my view the most notable of these assumptions is that the effects of

	sedentary time on mortality are constant by age, gender and other demographic and behavioral characteristics. … 6. Given that the average sedentary time is nearly 8 hours/d, as measured by accelerometer, it seems worth commenting on the magnitude of population behavior change needed to achieve the potential increase in life-expectancy. David Berrigan and Richard P. Troiano References Amount of time spent in sedentary behaviors in the United States, 2003-2004. Matthews CE, Chen KY, Freedson PS, Buchowski MS, Beech BM, Pate RR, Troiano RP. Am J Epidemiol. 2008 Apr 1;167(7):875-81. Sedentary behaviors and health outcomes among adults: a systematic review of prospective studies. Proper KI, Singh AS, van Mechelen W, Chinapaw MJ. Am J Prev Med. 2011 Feb;40(2):174-82 Sedentary behaviors and subsequent health outcomes in adults a systematic review of longitudinal studies, 1996-2011. Thorp AA, Owen N, Neuhaus M, Dunstan DW. Am J Prev Med. 2011 Aug;41(2):207-15.

REVIEWER	Lennert Veerman, MD MPH PhD Senior Research Fellow, School of Population Health, The University of Queensland Australia I have no competing interests.
REVIEW RETURNED	27/01/2012

GENERAL COMMENTS	This is an interesting study on an important topic. It is well-written but I wonder if the PAF calculation cannot be simplified and have a few more questions about methods and presentation. While the PAF formula used does indeed require the exposure data to be from cases, the result is a rather inelegant construction with adjusted prevalence estimates of TV viewing. In burden of disease studies the following PAF formula is often used: (formula not able to be copied; please see www.who.int/healthinfo/global_burden_disease/metrics_paf/en/index.html or attached file version of this review), in which • Pi = proportion of population at exposure level i, current exposure • P'i = proportion of population at exposure level i, counterfactual or ideal level of exposure • RR = the relative risk at exposure level i • n = the number of exposure levels This would avoid having to estimate the prevalence among cases. Rockhill, Newman & Weinberg don't mention this variant of PAF but to my knowledge it produces valid estimates. Page 5, line 20: Why were RRs used that were adjusted only for age and sex? Judging by references 13 and 15, further adjustment for factors like smoking, alcohol use, physical activity, education and diet quality would like reduce the RRs by what looks at a glance like some 15%. This might lead to overestimation of the impact on life expectancy. This issue is not mentioned in the discussion section of the paper.

	Page 5, line 12: The description of the MEDLINE search is rather summary, but at least for TV viewing it is confirmed by reference 4 so I agree with the current wording. Page 5, line 42: For what age categories were these prevalence estimates by age calculated? The current text suggests a single category 18+, but that seems very crude. Page 6, line 4-12 & Table 2: Why not use weighted averages for the calculation of ratios? Page 6 line 23: Please add a reference to 'cause-deleted life table analysis'. (I wasn't familiar with the term but learned via Google that I must have applied the concept in reference 7.) Page 7, line 42-51: Separate results for men and women would be helpful. Page 8, line 53-55: This is not quite accurate. For television viewing only 2 out of the 3 studies had the same definition as NHANES; Wijndaele et al (which contributes over half the weight in the RRs) had a different definition, which would have led to an underestimation of the RR in the highest risk category as the average TV time would be lower in that category and higher in the reference category, compared to the other studies. This would lead to a downward bias in the effects on life expectancy. Page 9, line 44 and further: In addition, inaccurate measurement of sedentary activity In the source studies would have caused regression dilution bias, which leads to underestimation of the association with outcomes. Figure 1: The RRs (and 95% CI's) for the Patel and Katzmarzyk studies seem to have changed places.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1: David Berrigan and Richard P. Troiano Applied Research Program Division of Cancer Control and Population Sciences National Cancer Institute

COMMENT 1. The calculations are based on self reported prevalence of sitting and television viewing from 2005-2006 and 2007-2008 NHANES, a large health survey in the United States. It is not clear why prevalence based on TV came from 2005-2006 and sitting prevalence came from 2007-2008.
RESPONSE: The last time NHANES asked about TV viewing in adults was in 2005-06 which is why we used that wave of data (now they only ask children that question). The sitting question for adults was introduced in 2007-2008 which was the most recent data available when we submitted this paper. As an update, NHANES has now released the 2009-2010 data since we submitted this paper, so we have updated the analysis with the new prevalences.

COMMENT 2. Self report has many cognitive challenges as well as potential for recall bias. The authors discuss these issues. However, why not compare the calculations with similar calculations based on objectively measured sedentary time? NHANES 2003-2006 included an accelerometer component and estimates of sedentary time based on these objective measurements have already been published (Matthews et al. 2008). This paper would be much more interesting if it contrasted the estimated effects of sedentary time on life expectancy based on self reported versus objectively measured sedentary time.
RESPONSE: This is an important observation. We have added a statement to the limitations section regarding the potential for error and recall bias. However, we could not determine the best approach

to incorporate the objective monitoring data into the analysis as there is no common metric across the studies. In other words, we have estimates of sedentary time from the NHANES accelerometers (for example, hours/day at < 100 counts per minute), and on the other hand in the cohort studies we have categories of TV viewing or sitting, and associated relative risk estimates. There is no way we know to reconcile these two approaches to produce a PAR. Any cut-points we would apply to the accelerometry in an attempt to make it align with the cohort study data would be artificial. We have added a statement that future cohort studies need to incorporate objective measures of sedentary behavior as exposure variables, which would align with the surveillance data and allow for these types of analysis in the future.

COMMENT 3. The estimates of the mortality effects of sedentary time are based on five studies. Recent reviews by Proper et al (2011) and Thorp et al. (2011) come up with different numbers of salient studies. More detail concerning the inclusion/exclusion criteria for this meta-analysis would be helpful.
RESPONSE: We have checked the Proper et al. (2011) and Thorp et al. (2011) studies. The Proper et al. study reviewed only three papers on sedentary behavior and mortality (p. 178) – two of them (the high quality studies) were in our meta-analysis (Katzmarzyk et al., Dunstan et al.), and the third low quality study (Graff-Iversen et al., 2007) did not assess the independent effect of sedentary behavior on mortality, rather they compared classes of occupational physical activity (OPA) ranked from sedentary (reference), light, moderately heavy, to heavy. This approach assumes the sedentary group is really the low end of physical activity rather than a distinct behavior like sitting or television viewing which is why we did not include it. In the Thorp et al. review, they identified 7 papers on sedentary behavior and mortality (p. 209), 5 of which were the ones reported in our study. The Warren et al. paper reported only CVD mortality (not all-cause mortality) as an outcome in men only, and so we did not include it. The Inoue et al. study reported results separately for men and women only, and adjusted for a multitude of covariates. We were not able to obtain the required age- and sex-adjusted RR estimates from the authors. Thus, our final slate of studies matches what has been presented in these other reviews. We have added some details around the keywords used for the PubMed searches as well as some inclusionary criteria.

COMMENT 4. In the discussion on page 9, the authors note that “assumptions had to be made when estimating the exposure levels in NHANES.” These assumptions should be described in the Methods.
RESPONSE: We have added the following section when describing the estimation of prevalences of sitting in NHANES in relation to the exposure categories in the cohort studies (page 7):
“Thus, three categories of exposure were used in each cohort study, and the prevalence of sitting categories from NHANES were obtained for three groups (<3 h, 3-5.9 h, and ≥6 h/day). However, given that the exposure categories from the Canadian cohort study were not quantifiable in terms of absolute hours/day, some misclassification may have occurred when combining the results.”

COMMENT 5. Perhaps the analysis could be illustrated by a figure of some kind. Such a figure might serve highlight some of the assumptions of the cause deleted life table approach as implemented here. In my view the most notable of these assumptions is that the effects of sedentary time on mortality are constant by age, gender and other demographic and behavioral characteristics.
RESPONSE: Unfortunately we have been unable to design a figure that would be appropriate, but in lieu of this we have added this assumption to the limitations paragraph as follows:
“Our analysis estimated the overall gains in life expectancy at the population level, and assumes that the effects of sedentary time on all-cause mortality are consistent across age and demographic sub-groups of the population.”

COMMENT 6. Given that the average sedentary time is nearly 8 hours/d, as measured by accelerometer, it seems worth commenting on the magnitude of population behavior change needed

to achieve the potential increase in life-expectancy.
RESPONSE: This is a good point. We have added a statement to that effect in the concluding comments:
"Given that the results from objective monitoring of sedentary time in NHANES has indicated that adults spend an average of 55% of their day engaged in sedentary pursuits26, a significant shift in behavior change at the population level is required to make demonstrable improvements in life expectancy."

Reviewer 2: Lennert Veerman, MD MPH PhD
Senior Research Fellow, School of Population Health, The University of Queensland Australia

COMMENT 1. While the PAF formula used does indeed require the exposure data to be from cases, the result is a rather inelegant construction with adjusted prevalence estimates of TV viewing. In burden of disease studies the following PAF formula is often used:
(formula not able to be copied; please see www.who.int/healthinfo/global_burden_disease/metrics_paf/en/index.html or attached file version of this review), in which
• Pi = proportion of population at exposure level i, current exposure
• P'i = proportion of population at exposure level i, counterfactual or ideal level of exposure
• RR = the relative risk at exposure level i
• n = the number of exposure levels

This would avoid having to estimate the prevalence among cases. Rockhill, Newman & Weinberg don't mention this variant of PAF but to my knowledge it produces valid estimates.
RESPONSE: We have investigated the new approach to quantifying disease burden as you have described. The formula you have provided uses a counterfactual approach in which it is not assumed that one can reduce exposure to zero, but rather to some other hypothetical prevalence or distribution that can be estimated from the effects of intervention studies, or estimates of a meaningful biological floor. In essence, this formula relaxes the assumption of a "no-exposure" group as the reference, and instead allows you to input different counterfactual scenarios. While this approach has relevance for many modeling exercises, given that we would like to compare our results to existing estimates of attributable life expectancy from other risk factors, and to provide an estimate of the total burden of sedentary behavior on life expectancy, we feel that the approach we have used is the most appropriate. Further, given the paucity of data from randomized trials on the potential effectiveness of interventions to reduce sedentary behaviors, we would not feel comfortable deciding on minimal exposure levels using this counterfactual approach.

COMMENT 2. Page 5, line 20: Why were RRs used that were adjusted only for age and sex? Judging by references 13 and 15, further adjustment for factors like smoking, alcohol use, physical activity, education and diet quality would like reduce the RRs by what looks at a glance like some 15%. This might lead to overestimation of the impact on life expectancy. This issue is not mentioned in the discussion section of the paper.
RESPONSE: We have added this issue to the limitations paragraph:
"Each of the cohort studies provided multivariable-adjusted RR estimates for sedentary behavior and mortality using different combinations of covariates, and we chose to use summary RR estimates based on RR adjusted for age and sex in order to maintain consistency across studies. The degree to which this approach has yielded an overestimation of the independent effect of sedentary behavior on life expectancy is not known."

COMMENT 3. Page 5, line 12: The description of the MEDLINE search is rather summary, but at least for TV viewing it is confirmed by reference 4 so I agree with the current wording.

RESPONSE: Thank you. We have added some additional description to the MEDLINE search based on comments of the other reviewer as well.

COMMENT 4. Page 5, line 42: For what age categories were these prevalence estimates by age calculated? The current text suggests a single category 18+, but that seems very crude.
RESPONSE: Yes, it was a single age category for adults. This was necessary to represent the adult population, and to capture the age ranges of the cohort studies (Table 1).

COMMENT 5. Page 6, line 4-12 & Table 2: Why not use weighted averages for the calculation of ratios?
RESPONSE: This is a good point. Given that the larger cohort studies likely have better point estimate of prevalence ratio, we have recalculated using weighted averages rather than the straight averages. Given the homogeneity in prevalence ratios across studies (Table 2), this has resulted in less than a percentage point difference in the final average adjusted prevalences, and thus has not changed the main results of the study.

COMMENT 6. Page 6 line 23: Please add a reference to 'cause-deleted life table analysis'. (I wasn't familiar with the term but learned via Google that I must have applied the concept in reference 7.)
RESPONSE: We have added two references which explain the cause-deleted approach.

COMMENT 7. Page 7, line 42-51: Separate results for men and women would be helpful.
RESPONSE: We agree that separate results for men and women would be helpful; however, in some of the smaller cohort studies the analyses could not be stratified by sex, so sex-adjusted analyses were performed rather than sex-specific. This is why we present only the overall results, adjusted for age and sex, rather than se-speciifc results. This is the same approach as used in the recent meta-analysis by Grontved and Hu (JAMA 2011) on television viewing and all-cause mortality, as they were facing similar limitations.

COMMENT 8. Page 8, line 53-55: This is not quite accurate. For television viewing only 2 out of the 3 studies had the same definition as NHANES; Wijndaele et al (which contributes over half the weight in the RRs) had a different definition, which would have led to an underestimation of the RR in the highest risk category as the average TV time would be lower in that category and higher in the reference category, compared to the other studies. This would lead to a downward bias in the effects on life expectancy.
RESPONSE: This is a good point. We have added the following part of a sentence to that section to highlight this issue:
"..however, Wijndaele et al.19 used a lower threshold for the upper category (>3.6 h) which may have resulted in an underestimate of the effects of television viewing on life expectancy."

COMMENT 9. Page 9, line 44 and further: In addition, inaccurate measurement of sedentary activity In the source studies would have caused regression dilution bias, which leads to underestimation of the association with outcomes.
RESPONSE: This is a good point. We have added the following sentence to the limitations section of the discussion based on your feedback:
"Inaccuracies associated with the assessment of sedentary behavior using self-report methods in the cohort studies would have led to regression dilution bias, and resulted in under-estimates of the association with all-cause mortality."

COMMENT 10. Figure 1: The RRs (and 95% CI's) for the Patel and Katzmarzyk studies seem to have changed places.
RESPONSE: You are correct as they were transposed in the top half of the figure. This error has been corrected.

VERSION 2 – REVIEW

REVIEWER	Lennert Veerman, PhD Senior Research Fellow, School of Population Health, The University of Queensland, Australia I have no competing interests.
REVIEW RETURNED	09/02/2012

GENERAL COMMENTS	I have only one comment, and it falls in the category 'discretionary'. In their response to my suggestion for an alternative PAF formula, the authors state that "[i]n essence, this formula relaxes the assumption of a "no-exposure" group as the reference, and instead allows you to input different counterfactual scenarios." Logically this should not therefore restrict the analysis, yet the authors report they "would not feel comfortable deciding on minimal exposure levels using this counterfactual approach". However, they used such counterfactual scenarios in their paper: <3h/day of sitting and <2h/day of TV viewing. I therefore think that the use of 'Global Burden of Disease-style' PAF would have been feasible. That said, the current calculations may be a bit elaborate but they are valid.

REVIEWER	David Berrigan Biologist National Cancer Institute USA I have no competing interests to declare
REVIEW RETURNED	13/02/2012

The reviewer completed the checklist but made no further comment.