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Response to the letter titled ‘Double counting individuals in meta-analysis artificially inflates precision.’

Running Head: Light physical activity and mortality

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We thank Tarp and colleagues for their interest in our work. Regarding the issue of duplicate study effects, it is an interesting area of discussion given that more and more cohorts are making their data publicly available and replication of research questions inevitable (and important). Study duplication ranges from complete replication of all study measurements and study effects to complete independence of all study measures and study effects based on different sub-samples. Authors of each paper may come from various institutions and make different decisions (i.e. sample extraction, variable coding, covariates, and data analysis) on how best to analyse the data so quite easily produce different results from the same data set.

In the current meta-analysis, there were six studies from the National Health and Nutrition Examination Survey (NHANES) (baseline: 2003-2006 with mean follow-up: 6.3-6.8 years)¹⁻⁶, which were conducted based on different sub-samples (n ranging from 2295 to 5562) by different research groups using diverse methods, whereas Koster et al.'s study utilized the data from the 2003-04 cycle of the survey with 2.8yr follow-up period. It would be difficult to decide on which one to include or exclude. The exclusion of all the study effects from potentially duplicate studies may lead bias. Some researchers advocate only the “original” or “main” study be included in the meta-analysis if it is the earliest published paper or the study with the largest sample size ⁸. Tarp et al. recommend that it is better to select the study best fit to answer the specific research question or select the study which maximizes analytical power (e.g. the study with the longest follow-up). However, eliminating all relevant studies but one still has its own issues. The decision on which study is the “original”, “main”, or “best fit to answer” is subjective, which may create bias for the meta-analysis ⁹. Indeed, it is challenging to single out the most appropriate one for inclusion among the six studies from the same cycle of the NHANES with the similar follow-up.

To examine the influence of including the six potentially duplicate studies, we have

conducted additional sensitivity analyses (See the APPENDIX TABLE). In Model 1 to 6, we examined the relationships of time spent in objectively-measured light-intensity physical activity with all-cause mortality assessed using log-cubic random-effects meta-regression models. Each of the six NHANES studies were individually included in the meta-regression model with the remaining five studies respectively. Although, Models 1 and 2 were of borderline significance (p -values = 0.069 and 0.052), the results revealed a consistent pattern across models, suggesting time spent in daily LPA was associated with reduced risks of mortality in adults and older people.

Because the six studies were only performed based on sub-samples of the NHANES, it is better to aggregate the study effects of the independent studies to provide a less-biased estimate of that study population in NHANES¹⁰. Before running Model 7, the aggregate mean effects with 95% confidence intervals (< 3 hour [ref.], 3-5 hour, 5-7 hour, and 7+ hours per day) of the NHANES studies were calculated using subgroup analysis based on the six studies from NHANES. This step was the same as those in Table 2 of the present meta-analysis. Then, the calculated mean effects were incorporated into the meta-regression analysis as a single study. Model 7 demonstrated a significant log-cubic association between time spent in daily LPA and all-cause mortality. Although the coefficients (and standard errors) of LPA were slightly different across models, they did not alter the conclusion of the current meta-analysis.

Although additional sensitivity analyses have been conducted to re-examine the associations of LPA with mortality, which support the conclusion, we recognize that duplicate study effects in meta-analysis are a critical issue. We utilized aggregate effects to assess the robustness of the findings but we believe that a superior approach is to utilize individual participant data (IPD) meta-analysis rather than extracting summary data from study publications or from different investigators.

Conflict of Interests:

Dr. Po-Wen Ku, Dr. Mark Hamer, Dr. Ming-Chun Hsueh, and Dr. Li-Jung Chen declare that they have no conflict of interest relevant to the content of this letter.

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