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Title:

Reply to: Joint associations of smoking and television viewing time on cancer and cardiovascular disease mortality—Methodological issues

Date:

2017-05-01

Citation:

Grace, M. S., Lynch, B. M., Dillon, F., Barr, E. L. M., Owen, N. & Dunstan, D. W. (2017). Reply to: Joint associations of smoking and television viewing time on cancer and cardiovascular disease mortality—Methodological issues. *International Journal of Cancer*, 140 (9), pp.2170-2171. <https://doi.org/10.1002/ijc.30641>.

Persistent Link:

<https://hdl.handle.net/11343/292587>

Letter to the Editor**Reply to: Joint Associations of Smoking and Television Viewing Time on Cancer and
Cardiovascular Disease Mortality: Methodological Issues**

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Accepted Article

This is the author manuscript accepted for publication and has undergone full peer review but has not been through the copyediting, typesetting, pagination and proofreading process, which may lead to differences between this version and the [Version record](#). Please cite this article as [doi:10.1002/ijc.30641](https://doi.org/10.1002/ijc.30641).

Dear Editor,

We thank Drs Pakzad and Safiri for their interest in our recent findings showing a joint association of smoking and television viewing time on cancer mortality¹. Their comments appropriately point to the limitations of analysing cancer mortality as a combined outcome, as the strength and direction of the associations between television viewing time and cancer have been shown to vary between different cancer types². Consistent with that perspective, we acknowledge that combining all cancer outcomes for our analysis is not ideal. However, the small number of cancer outcomes in the Australian Diabetes, Obesity and Lifestyle Study restricted the cancer-specific analyses that we could perform. We attempted to address this question with a sensitivity analysis that examined lung cancer specific mortality, which accounted for 44% of cancer-related deaths in current-smokers. We showed similar trends toward higher lung cancer mortality risk for every additional hour of television viewing time per day, as for the combined cancer outcome. We accept the merits of addressing this concern in future studies with datasets that have greater numbers of cancer deaths and/or longer-term follow-up. A dataset with more cancer outcomes would support further analyses to investigate the contribution of TV viewing time to specific cancers, or to groups of cancers with similar aetiologies. For example, cancers caused by epigenetic factors, hormonal or nutrient imbalances (e.g. lack of vitamin D), inflammation, or other risk factors that may be mechanistically linked to sedentary behaviours such as television viewing. Employing other statistical methods such as hierarchical regression analysis³, and analytic methods that allow for time-dependent exposure and confounding such as marginal structural models and the g-formula⁴, may also help us to better understand the nature of the associations between exposures of interest and outcomes such as mortality.

Drs Pakzad and Safiri also queried whether the conditions for the proportional hazards assumption were met for this study, based on results presented in Figure 1. We wish to clarify

that the data presented in Figure 1 are the unadjusted values/models, and therefore do not represent the results on which the proportional hazards test was based. The assumptions required for proportional hazards were met, and these were assessed with graphs of log-log plots of the relative hazards by time and scaled Schoenfeld residuals.

Our study found that among smokers higher TV viewing time was significantly associated with cancer mortality. Combining all cancer outcomes in our analysis is likely to have resulted in an underestimation of the strength of the associations with specific cancer types that are jointly associated with television viewing time and smoking. Thus, a more refined analysis may have resulted in stronger associations in current smokers. We hope that our initial hypothesis-generating findings will encourage further exploration of the joint associations of various lifestyle factors with sedentary behaviour on disease and mortality outcomes, and the underlying mechanisms that drive these deleterious effects on health.

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