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## Mortality effects of hypothetical interventions on physical activity and TV viewing
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| **Corresponding Author:** | Yi Yang<br>Cancer Council Victoria<br>Melbourne, Victoria AUSTRALIA |
| **Corresponding Author Secondary Information:** | |
| **Corresponding Author's Institution:** | Cancer Council Victoria |
| **Corresponding Author's Secondary Institution:** | |
| **First Author:** | Yi Yang |
| **First Author Secondary Information:** | |
| **Order of Authors:** | Yi Yang |
| | Allison Hodge |
| | Pierre-Antoine Dugué |
| | Elizabeth Williamson |
| | Paul Gardiner |
| | Elizabeth Barr |
| | Neville Owen |
| | David Dunstan |
| | Brigid Lynch |
| | Dallas English |
| **Order of Authors Secondary Information:** | |

| | |
|---|---|
| **Abstract:** | Introduction<br><br>Long-term effects of physical activity and TV viewing on mortality have been inferred from observational studies. The associations observed do not allow inferences about the effects of population interventions and could be subject to bias due to time-varying confounding.<br><br>Methods<br><br>Using data from the Australian Diabetes, Obesity and Lifestyle Study, collected at three time points, we applied the parametric g-formula to estimate cumulative risks of death under hypothetical interventions on physical activity and/or TV viewing, while adjusting for time-varying confounding.<br><br>Results<br><br>In the 6,377 participants followed for 13 years from 2004-05 to death or censoring in 2017, 781 participants died. The observed cumulative risk of death was 12.2%. The most effective hypothetical intervention was to increase weekly physical activity to >300 minutes (RR=0.66, 0.46 to 0.86 compared with a 'worst-case' scenario; and RR=0.83, 0.73 to 0.94 compared with no intervention). Reducing daily TV viewing to <2 hours in addition to physical activity interventions did not show added survival benefits. Reducing TV viewing alone was least effective in reducing mortality (RR=0.85, 0.60 to 1.10 compared with the worst-case scenario; and RR=1.06, 0.93 to 1.20 compared with no intervention).<br><br>Conclusion<br><br>Our findings suggested that sustained interventions to increase physical activity could lower all-cause mortality over a 13-year period and there might be limited gain from intervening to reduce TV viewing time in a relatively healthy population. |

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# Mortality effects of hypothetical interventions on physical activity and TV viewing

Yi Yang, MPH [1,2] Allison M. Hodge, PhD [1,2] Pierre-Antoine Dugué, PhD [1,2,3] Elizabeth J. Williamson, PhD [4,5] Paul A. Gardiner, PhD [6,7] Elizabeth L.M. Barr, PhD [8,9] Neville Owen, PhD [10] David W. Dunstan, PhD [11,12] Brigid M Lynch, PhD* [1,2,11] Dallas R English, PhD * [1,2]

* Brigid M Lynch, PhD and Dallas R English, PhD contributed equally to this work.

[1] Cancer Epidemiology Division, Cancer Council Victoria, Melbourne, VIC, Australia. [2] Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, VIC, Australia. [3] Precision Medicine, School of Clinical Sciences at Monash Health, Monash University, Clayton, VIC, Australia. [4] Department of Medical Statistics, London School of Hygiene and Tropical Medicine, London, United Kingdom. [5] Farr Institute of Health Informatics Research, London, United Kingdom. [6] Centre for Health Services Research, The University of Queensland, Brisbane, QLD, Australia. [7] Mater Research Institute-UQ, Brisbane, QLD Australia. [8] Menzies School of Health Research, Darwin, NT, Australia. [9] Baker Heart and Diabetes Institute, Melbourne, VIC, Australia. [10] Behavioural Epidemiology, Baker Heart and Diabetes Institute, Melbourne, VIC, Australia. [11] Physical Activity Laboratory, Baker Heart and Diabetes Institute, Melbourne, VIC, Australia. [12] Mary MacKillop Institute for Health Research, Australian Catholic University, Melbourne, VIC, Australia.

**Corresponding author** Yi Yang, yi.yang@cancervic.org.au, +61 3 9514 6268
615 St Kilda Rd, Melbourne, VIC 3004, Australia

**ABSTRACT**

**Introduction** Long-term effects of physical activity and TV viewing on mortality have been inferred from observational studies. The associations observed do not allow inferences about the effects of population interventions and could be subject to bias due to time-varying confounding.

**Methods** Using data from the Australian Diabetes, Obesity and Lifestyle Study, collected at three time points, we applied the parametric g-formula to estimate cumulative risks of death under hypothetical interventions on physical activity and/or TV viewing, while adjusting for time-varying confounding.

**Results** In the 6,377 participants followed for 13 years from 2004-05 to death or censoring in 2017, 781 participants died. The observed cumulative risk of death was 12.2%. The most effective hypothetical intervention was to increase weekly physical activity to >300 minutes (RR=0.66, 0.46 to 0.86 compared with a 'worst-case' scenario; and RR=0.83, 0.73 to 0.94 compared with no intervention). Reducing daily TV viewing to <2 hours in addition to physical activity interventions did not show added survival benefits. Reducing TV viewing alone was least effective in reducing mortality (RR=0.85, 0.60 to 1.10 compared with the worst-case scenario; and RR=1.06, 0.93 to 1.20 compared with no intervention).

**Conclusion** Our findings suggested that sustained interventions to increase physical activity could lower all-cause mortality over a 13-year period and there might be limited gain from intervening to reduce TV viewing time in a relatively healthy population.

Keywords: time-varying confounding, hypothetical interventions, g-formula, cohort study

## Introduction

Both insufficient physical activity (i.e., not meeting physical activity recommendations) and sedentary behaviour (time spent sitting, as distinct from lack of physical activity) contribute to risk of chronic disease and mortality. In the absence of evidence from randomized trials to quantify the long-term effects of changes in physical activity and sedentary behaviour, understanding how they are jointly related to mortality could be enhanced by better exploiting data from observational studies (1).

Insufficient physical activity and time spent in sedentary behaviours, particularly television (TV) viewing, have been associated with higher all-cause mortality in observational studies (2-4). These studies have typically measured exposures and confounders at a single time point, so did not assess the possible impact of exposure changes over follow-up. We have previously highlighted (5) that in studies that used data from multiple time points, conventional regression analyses can be problematic in the presence of time-varying confounding when the values of confounding variables are influenced by past exposures (e.g. sedentary behaviour affects obesity status, which in turn affects physical activity at the next time point) (6, 7). When there is time-varying confounding, conditioning on confounders (e.g. obesity status) that also lie in a causal pathway in standard regression models can produce biased estimates (see Web Figure 1, which illustrates an example of time-varying confounding affected by prior exposure) (8). Alternative methods such as inverse probability weighting of marginal structural models have been used to estimate causal effects of physical activity while adjusting for such time-varying confounding (9-13). No published studies on sedentary behaviour with multiple observation points have accounted for time-varying confounding.

Insufficient physical activity and sedentary behaviour can be viewed as separate risk factors with distinct sociodemographic and behavioural contexts and correlates (14). Our aim was to estimate the effects of single or joint hypothetical interventions for insufficient physical activity and a common leisure-time sedentary behaviour, TV viewing, on all-cause mortality over an approximate 13-year period, while accounting for time-varying confounding, using the parametric g-formula. We used the parametric g-formula because it allows estimation of the causal effects of complex population interventions, which could inform policy more directly compared with a typical exposure effect (15).

## Methods

### Study population

The Australian Diabetes, Obesity and Lifestyle Study (AusDiab) is a population-based cohort study conducted in the six states and the Northern Territory of Australia. Details about the cohort have been described (16). Briefly, participants aged at least 25 years were recruited in 1999-2000 (T0), then followed up in 2004-05 (T1), and 2011-12 (T2). Each data collection involved an initial household interview, followed by a biomedical examination and the administration of questionnaires. In the present study, we used T1 (2004-05) as baseline in order to have information on pre-baseline exposure and confounder history. Participants who attended T1 data collection (n=6,400) were included in this analysis. Participants who were pregnant (n=23) at data collections were excluded, which left 6,377 participants eligible for the analysis. The study was approved by the Ethics Committee of the International Diabetes Institute.

## Covariate measurements

Self-reported frequency and duration of leisure-time physical activity during the previous week was measured using the Active Australia Survey (17). The questions have been shown to have good reliability and validity (17). Physical activity consisted of walking for recreation or transport, moderate-intensity and vigorous-intensity physical activity at leisure-time. Weekly physical activity time was calculated as the total time spent walking continuously for $\geqslant$ 10 minutes or performing moderate physical activity, plus double the time spent in vigorous physical activity.

The total time spent watching TV or videos in the past 7 days was self-reported, excluding time when TV viewing and other activities (such as preparing a meal or doing other household chores) were being undertaken at the same time. This method has been shown to provide reliable and valid estimates of TV viewing time among adults (18). Average daily TV viewing hours was calculated.

Information on demographic attributes, history of health conditions, and self-reported general health was obtained by an interviewer-administered questionnaire (16). Alcohol and dietary intake were assessed using a self-administered, validated food frequency questionnaire (19). Mediterranean diet score was computed and used as a measure of overall diet quality (20). Waist circumference was measured by trained staff (16).

## Death ascertainment

Vital status and date of death were determined by linkage to the Australian National Death Index. Participants were followed until the date of death or administrative end of follow-up on 17 April 2017.

## Hypothetical interventions

We considered the following hypothetical interventions at T1 and T2, based on guidelines for physical activity (21) and the associations between TV viewing time and metabolic biomarkers (22-24) (No.2 to No.6 in Table 2): increasing weekly physical activity to sufficient (i.e. 150 to 300 minutes) if insufficiently active (i.e. <150 minute); increasing weekly physical activity to optimal (i.e. >300 minutes) for all participants; reducing daily TV viewing to <2 hours for all participants; increasing weekly physical activity to sufficient if insufficiently active and reducing daily TV viewing to <2 hours; and, increasing weekly physical activity to >300 minutes and reducing daily TV viewing to <2 hours for all participants.

In addition, for comparison, we considered a no-intervention scenario in which physical activity level and TV viewing time were allowed to evolve naturally (typically referred to as the 'natural course', No.0 in Table 2), and a scenario where weekly physical activity decreased to less than 30 minutes and daily TV viewing increased to 4 hours or more for all participants (i.e. worst-case scenario, No. 1 in Table 2).

## Statistical analysis

We used the parametric g-formula to estimate the 13-year cumulative risk of death under various hypothetical interventions on physical activity and/or TV viewing. The parametric g-formula is a generalization of standardization for time-varying exposures and confounders and can be used to estimate the standardized risk of death for hypothetical interventions under the assumptions of no unmeasured confounding, no measurement error and no model misspecification (7). The standardized risk is estimated by a weighted average of the risks of death conditional on the given intervention and the observed confounder history. The weights are probability distribution functions of the time-varying confounders estimated using parametric regression models. The weighted average is approximated through Monte Carlo simulation (25-27). We implemented the parametric g-formula in two steps. First, parametric models were fitted to model conditional probabilities of physical activity, TV viewing, and each of the following time-varying confounders in the order listed: history of high cholesterol, high blood pressure, heart disease, and diabetes, self-reported general health status, waist circumference, Mediterranean diet score, smoking status, and alcohol intake. The models also included the following time-fixed confounders: sex, baseline age, quintiles of an area-based index of relative socio-economic advantage and disadvantage, country of birth, and level of education (see Web Table 1 for details of models). These models were then used to simulate risk of death while setting physical activity and TV viewing to a specified intervention level in a Monte Carlo sample of the same size: 1) T0 and T1 confounder values were retained for all participants; T1 physical activity and TV viewing values were set to a specific level if part of an intervention; 2) risk of death before T2 was simulated; 3) for participants simulated to remain alive at T2: physical activity and TV viewing were set to a specific level if part of an intervention, T2 values of confounders were simulated by comparing the predicted probability of the confounder value to a value randomly drawn from a standard uniform distribution, and risk of death from T2 to the end of follow-up was simulated; 4) cumulative risk of death (i.e. 13-year risk) was calculated as:

$$P_{\text{13-year}} = P_{\text{death before T2}} + (1 - P_{\text{death before T2}})\, P_{\text{death after T2}}.$$

For each hypothetical intervention, we compared the estimated 13-year risk of death with the risk under the natural course (i.e. no-intervention scenario) and the risk under the worst-case scenario by calculating the risk ratios (RR) and risk differences (RD). We conducted the analyses separately in female and male participants to examine the possibility of effect heterogeneity by sex. We also compared simulated risk of death under the natural course with the observed risk as an informal validation of correct gross model specification.

Multiple imputation by chained equations (MICE) was used to impute missing data (due to missing response to the questionnaire, or missing T2 attendance for those who were still alive at T2). For each hypothetical intervention, point estimates were averaged over 40 imputed datasets; For the main analysis, 500 bootstrap samples were drawn for each imputed data set to estimate the standard errors and 95% confidence intervals were calculated using Rubin's rule (28, 29); for sensitivity analyses, 200 bootstrap samples were used.

For comparison with a conventional approach, Cox regression with age as the time scale was used to estimate hazard ratios for mortality associated with baseline TV viewing and physical activity, adjusting for baseline confounders.

Statistical analyses were performed using Stata version 14.2 (StataCorp, Texas, USA), and Stata version 15 on the University of Melbourne's high performance computing platform (30).

## Results

A total of 6,377 participants (54.7% female) were eligible. During 13 years (73,518 person years) of follow-up, 781 participants died (373 pre-T2 and 408 post-T2). Of participants who were alive at T2 (n=6,004), 20% did not attend T2 data collection.

Table 1 shows the characteristics of eligible participants at baseline (T1), and the potential time-varying confounders pre- and post-baseline. Mean age at baseline was 56.5 years. Three quarters (75.9%) were born in Australia or New Zealand and 40.2% had tertiary education. At baseline, more than half of the sample were sufficiently active (57%) or watched less than 2 hours of TV

(54%) (Table 1). Active participants tended to spend less time watching TV daily, although the differences were not large (Figure 1).

Table 2 shows the 13-year risks of death under various hypothetical interventions. The simulated 13-year risk of death under no intervention (12.1%) was very similar to the observed risk (12.2%), indicating that the models were correctly specified overall. The hypothetical intervention that reduced 13-year risk of death the most was to improve physical activity to >300 mins/week (RR=0.83, 0.73 to 0.94 compared with the natural course; and RR=0.66, 0.46 to 0.86 compared with the worst-case scenario), followed by improving physical activity to 150-300 mins/week for insufficiently active participants (RR=0.92, 0.82 to 1.01 compared with the natural course; and RR=0.73, 0.52 to 0.94 compared with the worst-case scenario). The average percentages of participants who needed to improve their physical activity were 65.2% and 42.1%, respectively for the two interventions. The intensive physical activity intervention would have prevented 20 deaths (CI: 7 to 33 deaths) per 1000 people in a 13-year period compared with not intervening. Reducing daily TV viewing to < 2 hours alone was the least effective intervention for lowering mortality (RR=1.06, 0.93 to 1.20 compared with the natural course; and RR=0.85, 0.60 to 1.10 compared with the worst-case scenario). Reducing daily TV hours jointly with any of the physical activity interventions required more people changing their behaviours (average of 80.7% and 68.2%, respectively), while not lowering the risk further.

Table 3 shows the 13-year risk of death in male and female participants under the natural course, the worst-case scenario, and the joint intensive intervention. The effect of hypothetical interventions on mortality (i.e. risk ratios) appeared to be similar for male and female participants. However, population risk difference was larger in males than in females because of higher absolute risks under the natural course.

We assumed correct ordering of exposures and time-varying confounders in our models. Our sensitivity analysis showed that results were robust to various modelling orders (see Web Table 2).

We found that the usual method of analysis, which used only baseline data in a Cox regression model underestimated the benefit of sustained higher physical activity compared with the g-formula, but the effect of TV viewing on all-cause mortality estimated from the g-formula was similar to the effect estimated from the Cox regression (see Web Figure 2, which shows the comparison of results estimated by g-formula and Cox regression ).

## Discussion

Our results suggest that in this cohort of adults, mortality could have been lowered by sustained interventions that increased physical activity. The intervention that appeared most effective to reduce mortality compared with no intervention was to increase weekly physical activity to >300 minutes (the intensive physical activity intervention), followed by increasing physical activity to 150-300 minutes/week in people who were insufficiently active (the moderate physical activity intervention). Interventions that reduced TV viewing time alone or in addition to physical activity interventions did not show added mortality benefits.

Although the intensive physical activity intervention was the most effective in reducing mortality, it required more participants to modify their behaviour modification to achieve the change (on average, 65% of participants needed to modify their physical activity levels at each time point) compared with the moderate physical activity intervention (42% on average needs to change). A systematic review found that relative reduction in all-cause mortality associated with higher physical activity was greater for females than for males (31), the effects of the hypothetical interventions on relative reduction in mortality were similar for females and males in our study.

Like other analyses of observational data, these estimates are based on the assumptions of no unmeasured confounding, no measurement error, and no model misspecification. We cannot exclude the possibility of unmeasured confounding despite adjusting for several important confounders. Self-reported time spent in physical activity and TV viewing are subject to measurement error. However, the questionnaires used in our study were previously shown to have good reliability and acceptable validity for estimates of the true exposure level (17, 18). We were able to closely reproduce the observed risk of death under the natural course, which is a necessary condition for no overall model misspecification under no intervention. The parametric g-formula requires fitting multiple models, therefore it may be more sensitive to violations of the above assumptions as violation in one model may accumulate through the others (25). Finally, the parametric g-formula is subject to the 'g-null paradox', i.e. the null hypothesis, (in our case, this is that interventions on physical activity and TV viewing have no effect on all-cause mortality), even if true, will be rejected in a large enough sample because the estimated value of the g-formula for the outcome generally depends on the exposure history (32). However, in practice, the g-null paradox is of less concern compared with typical random variability (33).

Current public health guidelines recommend minimizing sedentary behaviour and doing at least 150 mins/week of moderate-to-vigorous-intensity physical activity, or 300 mins/week for additional health benefit (34-36). These recommendations are mainly based on studies of associations between exposures at a single time point and risk of health outcomes such as cardiovascular health and cancer (35). Our study, on the other hand, estimated the potential impact on mortality had these two risk factors been altered by sustained population interventions. This is the key strength of our study, because it is rarely feasible to estimate such causal effects for a generally healthy population through randomized controlled trials (1). Our finding demonstrated that using a single measurement of physical activity is likely to underestimate the protective effects of physical activity. This may stimulate additional public health expenditure into physical activity promotion. Health promotion programmes frequently incorporate physical activity promotion into programmes address obesity prevention or reduction. Our research (which accounts for obesity-related time-varying confounding) highlights that physical activity itself is important for longevity.

Previous findings from the AusDiab study reported that watching ≥ 4 hours of TV daily was associated with higher all-cause mortality (37). Our Cox model showed a weaker association in the same direction between TV viewing time at T1 and all-cause mortality (See Web Figure 2). This could be partly because the previous study used T0 as baseline, whereas we used T1 as baseline. Our sample was smaller due to loss to follow-up between T0 and T1, and healthier. In our sample where daily TV viewing hours were already below two hours for more than half of the participants, we estimated no further survival benefit by intervening on this exposure. Over the 12 years between T0 (1999/2000) and T2 (2011/2012), there was an expansion of television viewing options, and other domestic entertainment and screen-based technologies, which may have reduced the relevance of our exposure variable. Although our estimates are not directly comparable to results from studies using conventional regression approaches, our findings and those of studies using regression approaches suggest protective effects of physical activity on mortality (31). Furthermore, we found that using only baseline data could underestimate the potential benefit of long-term physical activity.

Although we used repeatedly measured exposure data, the analyses would have benefited from more time points at regular intervals, which are more representative of sustained interventions over time. We coarsened the time spent in physical activity and TV viewing into categories relevant to current public health guidelines. This may affect the interpretation of our findings because of multiple versions of treatment (38). For example, our hypothetical intervention. "increasing physical activity to > 300 mins/week" can be achieved by increasing physical activity to 301 minutes or to 400 minutes through increasing activity duration or intensity over a week. Our estimates can be interpreted as a weighted average of the effects of the different versions, weighted by the probability of each version naturally arising within the population (38, 39). It should be noted that our estimates may not be generalizable to populations with different distributions of physical activity and TV viewing level. Results from the Australian National Health Surveys showed that the percentage of Australian adults with sufficient physical activity (i.e. ⩾ 150 mins/week ) remained low from 1989 to 2011 (39% in 1989 to 41% in 2011) (40). The hypothetical interventions we considered may have a greater benefit on lowering mortality in the general population than in our sample where close to 60% can be classified as 'sufficiently active'.

In conclusion, our findings suggest that sustained interventions on physical activity could lower all-cause mortality over a 13-year period, and that there might be limited gain from intervening on TV viewing time in a relatively healthy population.

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YY, AMH, PAD, BML, and DRE designed the study. YY performed the statistical analysis with support from EJW.  YY, AMH, PAD, BML, and DRE drafted the manuscript. PAG, ELMB, NO, and DWD contributed to the data interpretation and provided critical feedback for each draft. All authors read and approved the final manuscript.

## Conflict of interest

The authors declare that they have no relationship with companies or manufacturers who will benefit from the results of the present study. The results of the present study do not constitute endorsement by ACSM. The results of the study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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Tables and Figures

**Table 1. Characteristics of participants included in the analysis, Australia**

| | 1999-2000 (T0) N=6377 | | 2004-05 (T1) N=6377 | | 2011-12 (T2) N=4785[a] | |
|---|---|---|---|---|---|---|
| **Time-fixed covariates** | | | | | | |
| Baseline age (years), mean(SD) | | | 56.5 | (12.8) | | |
| Sex, N(%) | | | | | | |
| Male | | | 2891 | (45.3) | | |
| Female | | | 3486 | (54.7) | | |
| Born in Australia/New Zealand, N(%) | | | 4839 | (75.9) | | |
| The Index of Relative Socio-economic Advantage and Disadvantage (IRSAD), N(%) | | | | | | |
| 1 (greatest disadvantage) | | | 1084 | (17.3) | | |
| 2 | | | 1296 | (20.7) | | |
| 3 | | | 1291 | (20.6) | | |
| 4 | | | 1204 | (19.2) | | |
| 5 (greatest advantage) | | | 1395 | (22.2) | | |
| Level of education, N(%) | | | | | | |
| University or technical institution | | | 2561 | (40.2) | | |
| Completed high school | | | 1460 | (22.9) | | |
| Some high school | | | 1966 | (30.8) | | |
| Primary or never attended school | | | 390 | (6.1) | | |
| Baseline height(cm), mean(SD) | | | 167.6 | (9.6) | | |
| **Time-varying covariates** | | | | | | |
| Weekly Physical activity, N(%) | | | | | | |
| < 30 minutes | 1257 | (19.9) | 1099 | (17.4) | 729 | (15.8) |
| 30 to 149 minutes | 1686 | (26.7) | 1626 | (25.7) | 1127 | (24.4) |
| 150 to 300 minutes | 1368 | (21.6) | 1480 | (23.4) | 1074 | (23.3) |
| > 300 minutes | 2015 | (31.9) | 2118 | (33.5) | 1680 | (36.4) |
| Daily TV viewing time, N(%) | | | | | | |
| < 2 hours | 3655 | (57.7) | 3385 | (53.6) | 2030 | (52.7) |
| 2 to 4 hours | 2225 | (35.1) | 2340 | (37.0) | 1478 | (38.3) |
| ≥ 4 hours | 459 | (7.2) | 595 | (9.4) | 347 | (9.0) |
| Mediterranean Diet Score, N(%) | | | | | | |
| 0-3 | 1870 | (29.3) | 1922 | (30.7) | 1067 | (29.7) |
| 4-6 | 3766 | (59.1) | 3695 | (59.0) | 2127 | (59.3) |
| 7-9 | 741 | (11.6) | 651 | (10.4) | 394 | (11.0) |
| Waist circumference[b], N(%) | | | | | | |
| Normal | 2500 | (39.6) | 2120 | (33.3) | 1057 | (26.8) |
| Increased risk | 1641 | (26.0) | 1654 | (26.0) | 1007 | (25.5) |
| Greatly increased risk | 2173 | (34.4) | 2584 | (40.6) | 1879 | (47.7) |

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Tables and Figures

## Table 1. Characteristics of participants included in the analysis, Australia (continued)

| | | | | | | |
|---|---|---|---|---|---|---|
| Smoking status, N(%) | | | | | | |
| Never smoker | 3686 | (58.8) | 3527 | (58.0) | 2657 | (59.9) |
| Former smoker | 1858 | (29.6) | 1982 | (32.6) | 1517 | (34.2) |
| Current smoker | 723 | (11.5) | 568 | (9.3) | 260 | (5.9) |
| Alcohol intake (g/day), N(%) | | | | | | |
| 0 g/day (Male & Female) | 940 | (14.7) | 836 | (13.3) | 481 | (13.4) |
| 1-39(Male)/1-19(Female) | 4571 | (71.7) | 4470 | (71.3) | 2537 | (70.7) |
| 40-59(Male)/20-39(Female) | 627 | (9.8) | 683 | (10.9) | 411 | (11.5) |
| 60+(Male)/40+(Female) | 239 | (3.7) | 279 | (4.5) | 159 | (4.4) |
| Self-reported general health, N(%) | | | | | | |
| Excellent | 603 | (9.5) | 689 | (10.9) | 426 | (10.7) |
| Very Good | 2346 | (37.0) | 2335 | (36.9) | 1522 | (38.3) |
| Good | 2633 | (41.5) | 2460 | (38.8) | 1552 | (39.1) |
| Fair | 693 | (10.9) | 755 | (11.9) | 422 | (10.6) |
| Poor | 74 | (1.2) | 95 | (1.5) | 51 | (1.3) |
| History of health conditions, N(%) | | | | | | |
| High cholesterol | 1714 | (27.0) | 2654 | (41.8) | 3044 | (58.1) |
| High blood pressure | 1690 | (26.6) | 2399 | (37.7) | 2666 | (51.5) |
| Diabetes | 276 | (4.3) | 512 | (8.0) | 629 | (12.9) |
| Heart conditions | 443 | (7.0) | 559 | (8.8) | 218 | (4.6) |

Numbers across categories for some variables did not add up because of missing values.

[a] Number of participants attended T2, before multiple imputation was applied to impute missing data due to missing T2 attendance for those who were still alive at T2. [b] Normal: <94cm (male) or <80cm (female); increased risk: 94cm to <102cm (male) or 80cm to <88 cm (female); greatly increased risk: ≥102cm (male) or ≥88 (women).

**Mortality effects of hypothetical interventions on physical activity and TV viewing**

Tables and Figures

## Table 2. Risks of death under hypothetical interventions using the parametric g-formula

| No. | Interventions | | 13-year risk of death (%), 95% CI | Population risk difference (%), 95% CI | Population risk ratio, 95% CI | Risk difference (%), 95% CI | Risk ratio, 95% CI | Average % needed intervention[a] |
|---|---|---|---|---|---|---|---|---|
| 0 | Natural course | No intervention | 12.1 (10.9 to 13.2) | Reference | Reference | | | 0 |
| 1 | Worst-case scenario | Reducing physical activity to <30 mins/week, and increasing TV viewing to ≥4 hrs/day for all | 15.2 (11.6 to 18.9) | 3.2 (-0.4 to 6.8) | 1.26 (0.96 to 1.57) | Reference | Reference | 97.6 |
| 2 | Physical activity only, moderate | Increasing physical activity to 150-300 mins/week if <150 mins/week | 11.1 (9.7 to 12.4) | -1.0 (-2.2 to 0.2) | 0.92 (0.82 to 1.01) | -4.2 (-8.2 to -0.2) | 0.73 (0.52 to 0.94) | 42.1 |
| 3 | Physical activity only, intensive | Increasing physical activity to >300 mins/week for all | 10.0 (8.6 to 11.5) | -2.0 (-3.3 to -0.7) | 0.83 (0.73 to 0.94) | -5.2 (-9.3 to -1.1) | 0.66 (0.46 to 0.86) | 65.2 |
| 4 | TV viewing only | Reducing TV viewing to <2 hrs/day if ≥2 hrs/day | 12.8 (11.1 to 14.6) | 0.8 (-0.9 to 2.4) | 1.06 (0.93 to 1.20) | -2.4 (-6.6 to 1.8) | 0.85 (0.60 to 1.10) | 48.4 |
| 5 | Joint, moderate | Intervention No. 2 and No.4 | 11.6 (9.8 to 13.3) | -0.5 (-2.1 to 1.1) | 0.96 (0.83 to 1.09) | -3.7 (-8.0 to 0.7) | 0.76 (0.52 to 1.01) | 68.2 |
| 6 | Joint, intensive | Intervention No. 3 and No.4 | 10.5 (8.7 to 12.4) | -1.5 (-3.3 to 0.2) | 0.87 (0.73 to 1.02) | -4.7 (-9.2 to -0.2) | 0.70 (0.46 to 0.93) | 80.7 |

The observed 13-year risk of death was 12.2%; 500 bootstrap samples were drawn for each of the 40 imputed datasets to estimate the standard errors and 95% CIs. [a] Average percentage of participants who need to be intervened on at T1 and T2.

## Table 3. Risk of death under hypothetical interventions in women and men

| Interventions | 13-year risk of death (%), 95% CI | Population risk ratio, 95% CI | Population risk difference (%), 95% CI | Risk ratio, 95% CI | Risk difference (%), 95% CI |
|---|---|---|---|---|---|
| **Women** | | | | | |
| Natural course | 9.9 (8.4 to 11.3) | Reference | Reference | | |
| Worst-case scenario | 12.5 (8.0 to 16.9) | 1.27 (0.83 to 1.70) | 2.6 (-1.6 to 6.8) | Reference | Reference |
| Joint, intensive | 8.7 (6.1 to 11.3) | 0.88 (0.61 to 1.15) | -1.2 (-3.8 to 1.4) | 0.70 (0.31 to 1.09) | -3.8 (-9.6 to 2.0) |
| **Men** | | | | | |
| Natural course | 14.7 (13.1 to 16.4) | Reference | Reference | | |
| Worst-case scenario | 19.1 (12.9 to 25.2) | 1.30 (0.88 to 1.71) | 4.3 (-1.8 to 10.5) | Reference | Reference |
| Joint, intensive | 12.7 (9.7 to 15.7) | 0.86 (0.68 to 1.04) | -2.0 (-4.7 to 0.7) | 0.67 (0.36 to 0.98) | -6.4 (-14.0 to 1.3) |

The observed 13-year risk of death was 9.8% for women, and 15.2% for men; 200 bootstrap samples were drawn for each of the 40 imputed datasets to estimate the standard errors and 95% CIs.

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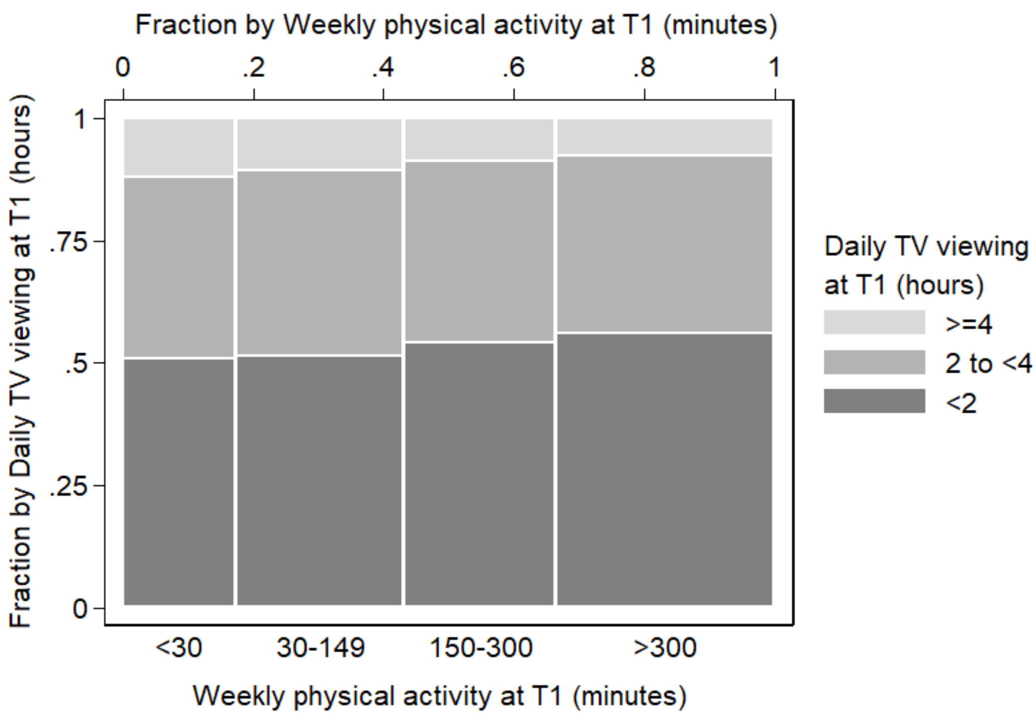
**Figure 1. Plot of daily TV viewing and weekly physical activity at baseline (T1)**



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Supplementary Documents.docx