Sitting Time and All-Cause Mortality Risk in 222 497 Australian Adults

Hidde P. van der Ploeg, PhD; Tien Chey, MA appStats; Rosemary J. Korda, PhD; Emily Banks, MBBS, PhD; Adrian Bauman, MBBS, PhD

Background: Prolonged sitting is considered detrimental to health, but evidence regarding the independent relationship of total sitting time with all-cause mortality is limited. This study aimed to determine the independent relationship of sitting time with all-cause mortality.

Methods: We linked prospective questionnaire data from 222 497 individuals 45 years or older from the 45 and Up Study to mortality data from the New South Wales Registry of Births, Deaths, and Marriages (Australia) from February 1, 2006, through December 31, 2010. Cox proportional hazards models examined all-cause mortality in relation to sitting time, adjusting for potential confounders that included sex, age, education, urban/rural residence, physical activity, body mass index, smoking status, self-rated health, and disability.

Results: During 621 695 person-years of follow-up (mean follow-up, 2.8 years), 5405 deaths were registered. All-cause mortality hazard ratios were 1.02 (95% CI, 0.95-1.09), 1.15 (1.06-1.25), and 1.40 (1.27-1.55) for 4 to less than 8, 8 to less than 11, and 11 or more h/d of sitting, respectively, compared with less than 4 h/d, adjusting for physical activity and other confounders. The population-attributable fraction for sitting was 6.9%. The association between sitting and all-cause mortality appeared consistent across the sexes, age groups, body mass index categories, and physical activity levels and across healthy participants compared with participants with preexisting cardiovascular disease or diabetes mellitus.

Conclusions: Prolonged sitting is a risk factor for all-cause mortality, independent of physical activity. Public health programs should focus on reducing sitting time in addition to increasing physical activity levels.

tions that involve prolonged sitting. A recent meta-analysis showed television viewing was associated with higher risks of type 2 diabetes mellitus, cardiovascular disease, and all-cause mortality. However, not many studies have looked at the effect of total sitting time on all-cause mortality. Establishing quantitatively the relationship between total sitting time and all-cause mortality is important from an etiological point of view and to inform public health programs because individuals might compensate for frequent sitting in one domain by less sitting in another domain. To our knowledge, 1 previous prospective cohort study has researched the relationship between sedentary time and all-cause mortality (n=83,034). However, the primary focus of that study was on physical activity, and undefined sedentary activity was assessed with a basic measure that classified subjects into the following 3 categories: less than 3, 3 to less than 8, and at least 8 h/d. The authors found a significant detrimental effect on all-cause mortality only for men with at least 8 h/d of sedentary activity compared with men with less than 3 h/d.

The present study focuses on the dose-response relationship between total sitting time and all-cause mortality and uses data from the prospective cohort 45 and Up Study. The objective of our study was to determine the independent relationship of sitting time with all-cause mortality in subjects 45 years or older residing in the state of New South Wales, Australia.

### METHODS

#### STUDY POPULATION

The analyses are based on data from 222,497 participants who completed a baseline questionnaire from February 1, 2006, through November 30, 2008, for the 45 and Up Study, a large-scale prospective cohort study of men and women 45 years or older from the general population of the state of New South Wales, Australia. Individuals 45 years or older were randomly sampled from the Medicare Australia database, through which national health care is administered and which includes all citizens and permanent residents of Australia and some temporary residents and refugees. Eligible individuals were mailed an invitation to participate, an information leaflet, the study questionnaire, a consent form (including consent for long-term follow-up through linkage of their data to data held in a variety of population databases), and a prepaid reply envelope. Participants joined the study by completing the questionnaire and consent form and mailing them to the study coordinating center. Approximately 11% of the entire New South Wales population 45 years or older was included in the final sample. A more detailed description of the 45 and Up Study can be found elsewhere. The present project was approved by the New South Wales Population and Health Services Research Ethics Committee (reference No. 2010/03/234).

#### STUDY VARIABLES

Information on exposures, including sitting time, was based on self-reported data from the 45 and Up Study baseline questionnaire (available at http://www.45andup.org.au). The main exposure variable, time spent sitting, was assessed with the question “About how many hours in each 24-hour day do you usually spend sitting?” This question is similar to the sitting mea-

### STATISTICAL ANALYSIS

The association between sitting and risk of death was analyzed using Cox proportional hazards regression models. Survival time, measured as the time from baseline to death or the censor point (December 31, 2010), was the outcome variable, with a categorical representation of sitting time as the exposure variable.

Sitting time was divided into the following 4 categories: 0 to less than 4, 4 to less than 8, 8 to less than 11, and 11 or more h/d. Hazard ratios (HRs) for each category of sitting time relative to less than 4 h/d and tests for trends across the 4 categories were calculated using Cox proportional hazards regression models. The population-attributable fraction of sitting to all-cause mortality was calculated using adjusted relative risks for the 4 categories of sitting time. Absolute all-cause mortality risks per 1000 person-years were calculated for combined categories of sitting and physical activity.

All Cox proportional hazards regression analyses were adjusted for sex, age, educational level, marital status, urban or rural residence, BMI, physical activity, and smoking status. To account for possible reverse causation, self-rated health and receiving help with daily tasks for a long-term illness or disability were also adjusted for in all Cox regression analyses. To maxi-

Potential confounding variables included sex, age, educational level, urban/rural residence, physical activity, body mass index (BMI; calculated as weight in kilograms divided by height in meters squared), smoking status, self-rated health, and disability. Total physical activity was assessed with the Active Australia Survey, which measures walking and other moderate- and vigorous-intensity physical activity and has acceptable reliability and validity. Body mass index was calculated from self-reported weight and height, which has shown excellent agreement with measured BMI categories within a subsample of the study. Participants were asked to report any previous diagnosis by a physician of heart disease, stroke, thrombosis, diabetes mellitus, and various cancers and whether they were current, past, or never smokers. Self-rated overall health was assessed with a single question on a 5-point scale (ranging from excellent to poor) from the 36-item Short Form Health Survey. Participants also recorded whether they needed regular help with daily tasks because of long-term illness or disability.

The outcome variable, all-cause mortality, was ascertained from the New South Wales Registry of Births, Deaths, and Marriages from February 1, 2006, through December 31, 2010. The mortality data were linked to the baseline data from the 45 and Up Study by the Centre for Health Record Linkage (Eveleigh, New South Wales, Australia) using probabilistic record linkage methods and commercially available software (ChoiceMaker; ChoiceMaker Technologies Inc). Manual clerical review was performed to check indeterminate matches (approximately 2%), with upper and lower probability cutoffs of 0.7973 and 0.2860, respectively. Evaluation of the accuracy of the overall linkage was determined by clerical review of samples of matched records. Quality assurance data show false-positive and false-negative rates of less than 0.5%.
mize statistical power, participants with missing values for any of the adjustment variables were assigned to a separate category for that variable. This method showed similar effect sizes to the analyses that were restricted to participants with no missing values on any of the adjustment variables. To determine whether the association between sitting and all-cause mortality differed between a priori-defined subgroups, we tested for interaction effects between sitting and sex, age, cardiovascular disease and diabetes, BMI, and physical activity using a likelihood ratio test that compared the model with and without the interaction term.

The Cox regression models were repeated for subgroups of participants with cardiovascular disease (including heart disease, stroke, and thrombosis) or diabetes mellitus and for participants who were considered (relatively) healthy with no cardiovascular disease, diabetes, or cancer (with the exception of nonmelanoma skin cancer). The Cox regression models were also repeated with stratification for BMI categories using World Health Organization criteria for underweight (13.0-18.4), healthy weight (18.5-24.9), overweight (25.0-29.9), and obese (30.0-60.0).\(^2\) All Cox regression results were presented as HRs (with 95% CIs). The assumption of proportionality (for sitting categories) was tested and met in the presence of other covariates in the full model. All analyses were conducted by two of us (H.P.v.d.P. and T.C.) using commercially available statistical software (SAS, version 9.1.3; SAS Institute, Inc). People with missing data for sitting, physical activity, or BMI were excluded from the analyses (16.6%), which resulted in a sample for all adjusted Cox proportional hazards regression analyses of 222,497 participants. Missing data for all other adjustment variables were included in the analyses as a separate category. Because of the relatively short mean follow-up, the whole group analysis was repeated with only participants who had more than 1 year of follow-up (n=219,628) to check for a potential confounding effect of occult disease at baseline.

### RESULTS

Descriptive statistics for the study cohort in relation to sitting time are presented in Table 1. Of the 222,497 participants, 52.4% were women, 62.0% were overweight or obese, 86.7% reported good to excellent health, 25.2% were sitting at least 8 h/d, and 75.0% met the 150-min/wk physical activity guideline. Durations of sitting time tended to be greater in the younger groups and among those with the highest educational levels, poorer self-rated health, requirements for help with daily tasks, lower physical activity levels, and higher BMI.

### SITTING AND ALL-CAUSE MORTALITY

During 621,695 person-years of observation (mean [SD] follow-up time, 2.8 [0.9] years), 5,405 deaths were registered. Table 2 presents the results from the Cox proportional hazards regression analyses, showing the relationship of sitting with all-cause mortality after adjusting for sex, age, educational level, marital status, urban or rural residence, physical activity, BMI, smoking status, self-rated health, and receiving help with daily tasks for a long-term illness or disability. All-cause mortality HRs were 1.02 (95% CI, 0.95-1.09), 1.15 (1.06-1.25), and 1.40 (1.27-1.55) for 4 to less than 8, 8 to less than 11, and 11 or more h/d of sitting, respectively, compared with less than 4 h/d. The trend for the 4 groups of sitting showed a significant HR for all-cause mortality of 1.11 (95% CI, 1.08-1.15), suggesting an 11% increase in all-cause mortality for an increase of 1 sitting category. The population-attributable fraction for sitting was 6.9%. Analysis of interaction effects showed that the relation of sitting time to mortality did not vary significantly according to participants' sex (P=.06), age (P=.21), level of physical activity (P=.39), BMI (P=.78), or cardiovascular disease and diabetes status (P=.18).

To check for potential confounding effects due to occult disease at baseline, the analysis for the whole sample was repeated including only subjects with more than 1 year of follow-up and including 3,958 deaths (n=219,628). The all-cause mortality HRs for sitting time were 1.03 (95% CI, 0.95-1.12), 1.16 (1.05-1.28), and 1.41 (1.25-1.59) for 4 to less than 8, 8 to less than 11, and at least 11 h/d, respectively, with less than 4 h/d as the reference category.

The Figure illustrates the combined relationship of sitting and physical activity with absolute all-cause mortality rates per 1,000 person-years and shows a clear dose-response relationship for sitting time and physical activity with all-cause mortality. It demonstrates that inactive participants with high levels of sitting had the highest mortality rate, and the strong relationship of increased sitting time to mortality persisted, even among participants with relatively high levels of physical activity. As expected, healthy participants had lower absolute all-cause mortality rates compared with participants with preexisting cardiovascular disease or diabetes, and increased physical activity and reduced sitting were associated with reduced rates in both groups.

The results show that prolonged sitting is significantly associated with higher all-cause mortality risk independent of physical activity. The population-attributable fraction of sitting time suggested that sitting was responsible for 6.9% of deaths. The association between sitting and all-cause mortality appears relatively consistent across women and men, age groups, BMI categories, and physical activity levels and across healthy participants compared with those with preexisting cardiovascular disease or diabetes mellitus.

Combined sitting and physical activity risk profiles showed clear dose-response relationships with all-cause mortality, with people who sit the most and perform no weekly physical activity having the highest all-cause mortality risk. Sitting less than 8 h/d and meeting the physical activity recommendation of the World Health Organization\(^2\) independently protected against all-cause mortality. The greater absolute mortality risk in individuals with existing cardiovascular disease, diabetes, overweight, or obesity means that the absolute mortality benefits from sitting less are likely to be greater in these groups.

Our findings help to further build the accumulating evidence around the association between sedentary behaviors and health. Previous analyses of prospective co-
hort data have suggested adverse associations between mortality and sitting time in specific subdomains, including work, transport, and leisure (mostly television viewing). Another study determined the relationship between total sedentary activity and all-cause mortality but found a detrimental relationship only for men and not for women. However, that study had a categorical measure of sedentary activity that had at least 8 h/d as the highest category, which is likely to have lacked sensitivity to detect the relationship with all-cause mortality. A recent systematic review also showed moderate evidence of an adverse association between sitting and type 2 diabetes mellitus but reported insufficient prospective evidence of associations with body weight, cardiovascular disease, or endometrial cancer. However, the authors stressed that sedentary behavior research is still in its infancy and that more high-quality prospective studies are needed. Another systematic review of the relationship between occupational sitting time and health outcomes suggested that individuals with more active jobs had lower all-cause or cardiovascular disease mortality risk than those with jobs that involved mostly sitting. However, a lack of accurate measures and the heterogeneity of study designs and findings made it difficult to draw definitive conclusions. In particular, the use of more accurate measures of sitting that include total sitting time and preferably the use of an objective measure has been recommended for future studies.

The adverse effects of prolonged sitting are thought to be mainly owing to reduced metabolic and vascular health. Prolonged sitting has been shown to disrupt metabolic function, resulting in increased plasma triglycer-
ide levels, decreased levels of high-density lipoprotein cholesterol, and decreased insulin sensitivity, which appear to be at least partially mediated by changes in lipoprotein lipase activity. It has also been suggested that sedentary behavior affects carbohydrate metabolism through changes in muscle glucose transporter protein content.3,30 Results from molecular biology and medical chemistry studies have suggested that physical activity and seden-
tary behavior have different influences on the body, supporting their independent effects on health.\textsuperscript{31} Our findings suggested not only an association between sitting and all-cause mortality that was independent of physical activity but, because the findings persisted after adjustment and stratification for BMI, one that also appears to be independent of BMI.

A limitation of the present study is the relatively short mean follow-up time of 2.8 years, which could have resulted in a potential confounding effect of occult disease at baseline. However, analyses were adjusted for self-rated health and disability at baseline, and findings persisted when data were restricted to a relatively healthy subgroup of the study population. Furthermore, the findings did not change materially after restriction of the data set to participants with at least 1 year of follow-up despite the fact that this resulted in exclusion of 26.8% of the deaths in the cohort. This finding suggests that reverse causality might not be a major factor in the observed relationships, especially given the acute nature of the exposure variable (ie, people who do not feel well will probably increase their sitting time, and a consequent substantial increase in sitting will likely be accompanied with a decrease in self-rated health). However, the possibility that reverse causality due to occult disease influenced findings to a certain extent cannot be excluded.

Another limitation was the use of self-report measures for the exposure variables, which could have resulted in some measurement error and most likely attenuation of HRs. Although the analyses were adjusted for known confounders, the potential for unmeasured confounding always exists. The main strengths of the present study were the large study population, the prospective nature of the analyses, the ability to link to death records, and virtually complete follow-up of participants.

Our findings add to the mounting evidence that public health programs should focus not just on increasing population physical activity levels but also on reducing sitting time, especially in individuals who do not meet the physical activity recommendation. The potential public health gains are substantial, because in the United States, less than half the adult population meets the physical activity rec-
New Exercise Prescription

Don’t Just Sit There: Stand Up and Move More, More Often

In their article, van der Ploeg and colleagues report important new findings from a large population-based study of Australian adults. They show total sitting time to be associated prospectively with all-cause mortality after accounting for many likely confounding variables, including leisure-time physical activity.

Increasing physical activity in adult populations is central to the prevention of obesity and the major chronic diseases. Traditionally, the focus has been on encouraging individuals to participate in moderate-to-vigorous physical activity (“health-enhancing exercise”) during their discretionary time, with a more recent emphasis on physically active transportation. 2 For example, an indi-