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

Hidde P. van der Ploeg, PhD; Tien Chey, MAppStats; 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.

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The benefits of a physically active lifestyle are established,[1,2] with physical inactivity estimated to account for 6% of global deaths.[2] The World Health Organization recommends that adults participate in at least 150 minutes of at least moderate-intensity aerobic physical activity throughout the week to reduce the risk of chronic disease, including cardiovascular disease, type 2 diabetes mellitus, and certain cancers.[3]

See Invited Commentary at end of article

Sedentary activities are defined as those incurring no more than 1.5 metabolic equivalents and include the specific behaviors of sitting and lying down. These behaviors are generally considered distinct from inactivity, which refers to a lack of moderate or vigorous physical activity (≥3 metabolic equivalents).[4] The health risks of sedentary behavior have not been as well researched as those of lack of physical activity but have recently received increasing attention.[5-8] Even when individuals engage in 150 min/wk of physical activity, increasing evidence suggests that what happens in the remaining approximately 6500 minutes of the waking week is important for health.

High volumes of sitting time have possible associations with increased risk of obesity, cardiovascular disease, diabetes, and cancer.[7,8] However, a recent systematic review concluded that additional high-quality prospective studies are needed to clarify the causal relationships between sedentary behaviors and health.[7]

Recent analyses of prospective studies have suggested that all-cause mortality is adversely associated with television viewing,[9-11] recreational screen time,[12] sitting during leisure time,[13] sitting in a car,[10] sitting during main activities (eg, work, school, and housework),[14] and occupa-

Author Affiliations: Sydney School of Public Health, University of Sydney (Dr van der Ploeg, Prof Bauman, and Ms Chey), and The Sax Institute (Dr Banks), Sydney, Australia; and National Centre for Epidemiology and Population Health, Australian National University, Acton, Australia (Dr Korda and Prof Banks).

tions that involve prolonged sitting.[15] A recent meta-analysis showed television viewing was associated with higher risks of type 2 diabetes mellitus, cardiovascular disease, and all-cause mortality.[16] 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).[17] 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.[17] 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.[17]

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.[18] 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.[18] The present project was approved by the New South Wales Population and Health Services Research Ethics Committee (reference No. 2010/05/234).

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 measure of the often-used International Physical Activity Questionnaire, which has shown acceptable reliability and validity.[19]

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,[20] which measures walking and other moderate- and vigorous-intensity physical activity and has acceptable reliability and validity.[21,22] 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.[23] 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.[24] Participants also recorded whether they needed regular help with daily tasks because of long-term illness or disability.[25]

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%.

STATISTICAL ANALYSIS

The association between sitting and risk of death was analyzed using Cox proportional hazards regression models.[26] 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.[27] Absolute all-cause mortality risks per 1000 person-years were calculated for combined categories of sitting and physical activity. For physical activity, the following 4 categories were used: no physical activity (0 min/wk), some physical activity but not meeting recommended levels (1-149 min/wk), meeting the minimum but less than twice the amount of the World Health Organization recommendation (150-299 min/wk),[3] and meeting at least twice the minimum recommended amount ($\geq$300 min/wk).

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 maximize 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).[28] 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.vdP. 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

STUDY POPULATION

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), 5405 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 3958 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 1000 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.

COMMENT

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[3] 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-

Table 1. Characteristics of the Cohort Participants by Time Spent Sitting[a]

Variable	Time Sitting, h/d, No. (% of Row) 0 to <4	4 to <8	8 to <11	≥11	All Groups, No. (% of Column)
All participants	58 534 (26.3)	107 994 (48.5)	41 646 (18.7)	14 323 (6.4)	**222 497** (100.0)
Sex					
Male	25 601 (24.2)	50 588 (47.8)	21 412 (20.2)	8254 (7.8)	**105 855** (47.6)
Female	32 933 (28.2)	57 406 (49.2)	20 234 (17.3)	6069 (5.2)	**116 642** (52.4)
Age, y					
45-54	17 950 (26.3)	28 861 (42.4)	15 557 (22.8)	5757 (8.5)	**68 125** (30.6)
55-64	19 707 (26.7)	35 466 (48.0)	13 797 (18.7)	4855 (6.6)	**73 825** (33.2)
65-74	12 988 (27.4)	26 023 (54.9)	6676 (14.1)	1749 (3.7)	**47 436** (21.3)
≥75	7889 (23.8)	17 644 (53.3)	5616 (17.0)	1962 (5.9)	**33 111** (14.9)
Educational level					
≤High school (low)	19 995 (28.4)	35 845 (51.0)	11 068 (15.7)	3439 (4.9)	**70 347** (32.0)
Middle	25 914 (27.4)	46 533 (49.2)	16 646 (17.6)	5421 (5.7)	**94 514** (43.0)
≥Completed university (high)	11 829 (21.5)	24 355 (44.2)	13 531 (24.6)	5330 (9.7)	**55 045** (25.0)
Marital status					
Married/de facto	45 033 (26.7)	82 207 (48.7)	31 054 (18.4)	10 395 (6.2)	**168 689** (76.2)
Other	13 161 (25.0)	25 223 (47.9)	10 379 (19.7)	3872 (7.4)	**52 635** (23.8)
Location of residence					
Rural	19 444 (29.9)	32 582 (50.1)	10 070 (15.5)	2922 (4.5)	**65 018** (29.2)
Urban	39 057 (24.8)	75 332 (47.9)	31 527 (20.0)	11 379 (7.2)	**157 295** (70.8)
BMI					
<18.5	846 (29.7)	1323 (46.5)	499 (17.5)	180 (6.3)	**2848** (1.3)
18.5 to <25.0	23 381 (28.6)	39 582 (48.5)	14 117 (17.3)	4562 (5.6)	**81 642** (36.7)
25.0 to <30.0	22 827 (25.9)	43 188 (49.0)	16 591 (18.8)	5591 (6.3)	**88 197** (39.6)
≥30.0	11 480 (23.0)	23 901 (48.0)	10 439 (21.0)	3990 (8.0)	**49 810** (22.4)
Smoking status					
Current smoker	4188 (26.5)	7526 (47.6)	2930 (18.5)	1158 (7.3)	**15 802** (7.1)
Ex-smoker	19 800 (24.7)	39 665 (49.5)	15 383 (19.2)	5334 (6.7)	**80 182** (36.1)
Never smoker	34 366 (27.3)	60 517 (48.1)	23 222 (18.4)	7789 (6.2)	**125 894** (56.7)
Self-rated health status					
Excellent	10 058 (29.5)	15 816 (46.3)	6314 (18.5)	1964 (5.8)	**34 152** (15.8)
Very good	21 997 (27.0)	39 966 (49.0)	14 902 (18.3)	4728 (5.8)	**81 593** (37.8)
Good	18 260 (25.5)	35 668 (49.8)	13 283 (18.5)	4476 (6.2)	**71 687** (33.2)
Fair	5526 (22.6)	11 770 (48.1)	5075 (20.7)	2099 (8.6)	**24 470** (11.3)
Poor	815 (19.3)	1709 (40.4)	1051 (24.8)	658 (15.5)	**4233** (2.0)
Help with daily tasks because of long-term illness or disability					
No	53 829 (26.6)	98 821 (48.8)	37 694 (18.6)	12 260 (6.1)	**202 604** (94.9)
Yes	2137 (19.6)	4757 (43.6)	2459 (22.6)	1547 (14.2)	**10 900** (5.1)
Physical activity, min/wk					
0	2802 (23.2)	4981 (41.2)	2737 (22.6)	1580 (13.1)	**12 100** (5.4)
1-149	10 203 (23.5)	19 784 (45.5)	9544 (22.0)	3935 (9.1)	**43 466** (19.5)
150-299	10 773 (24.0)	20 816 (46.4)	9762 (21.8)	3473 (7.7)	**44 824** (20.1)
≥300	34 756 (28.5)	62 413 (51.1)	19 603 (16.1)	5335 (4.4)	**122 107** (54.9)

Abbreviation: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).
[a]Percentages have been rounded and might not total 100.

hort data have suggested adverse associations between mortality and sitting time in specific subdomains, including work,[14,15] transport,[10] and leisure (mostly television viewing).[9-13,16] 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.[17] 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.[7] 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.[15] 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.[15,29]

The adverse effects of prolonged sitting are thought to be mainly owing to reduced metabolic and vascular health.[8] Prolonged sitting has been shown to disrupt metabolic function, resulting in increased plasma triglycer-

Table 2. Association Between Sitting and All-Cause Mortality Among Australian Adults 45 Years or Older[a]

Population	Sitting Time, h/d 0 to <4	4 to <8	8 to <11	≥11	Trend
All participants					
No. of deaths	1125	2489	1142	649	
HR (95% CI)	1.00 [Reference]	1.02 (0.95-1.09)	1.15 (1.06-1.25)	1.40 (1.27-1.55)	1.11 (1.08-1.15)
Women					
No. of deaths	381	836	403	248	
HR (95% CI)	1.00 [Reference]	1.06 (0.94-1.20)	1.24 (1.08-1.43)	1.62 (1.37-1.92)	1.17 (1.11-1.23)
Men					
No. of deaths	744	1653	739	401	
HR (95% CI)	1.00 [Reference]	1.00 (0.91-1.09)	1.12 (1.01-1.24)	1.32 (1.16-1.50)	1.09 (1.05-1.14)
Aged 45-54 y					
No. of deaths	70	131	77	42	
HR (95% CI)	1.00 [Reference]	1.09 (0.81-1.46)	1.16 (0.83-1.61)	1.43 (0.97-2.12)	1.11 (0.99-1.25)
Aged 55-64 y					
No. of deaths	164	327	133	85	
HR (95% CI)	1.00 [Reference]	1.08 (0.89-1.30)	1.05 (0.83-1.32)	1.47 (1.13-1.93)	1.10 (1.01-1.20)
Aged 65-74 y					
No. of deaths	257	575	232	101	
HR (95% CI)	1.00 [Reference]	1.02 (0.88-1.19)	1.30 (1.09-1.56)	1.36 (1.07-1.73)	1.13 (1.05-1.22)
Aged ≥75 y					
No. of deaths	634	1456	700	421	
HR (95% CI)	1.00 [Reference]	0.99 (0.91-1.09)	1.14 (1.02-1.28)	1.42 (1.25-1.62)	1.12 (1.08-1.17)
Healthy					
No. of deaths	325	718	290	157	
HR (95% CI)	1.00 [Reference]	1.11 (0.97-1.27)	1.23 (1.04-1.44)	1.45 (1.19-1.77)	1.12 (1.06-1.19)
Cardiovascular disease or diabetes mellitus					
No. of deaths	544	1246	610	385	
HR (95% CI)	1.00 [Reference]	0.96 (0.87-1.07)	1.10 (0.98-1.24)	1.42 (1.24-1.63)	1.12 (1.07-1.17)
Healthy weight					
No. of deaths	511	1092	474	252	
HR (95% CI)	1.00 [Reference]	1.02 (0.92-1.14)	1.13 (1.00-1.28)	1.33 (1.13-1.55)	1.09 (1.04-1.15)
Overweight					
No. of deaths	376	832	390	214	
HR (95% CI)	1.00 [Reference]	0.99 (0.88-1.12)	1.23 (1.06-1.42)	1.53 (1.29-1.83)	1.16 (1.10-1.22)
Obese					
No. of deaths	177	450	221	139	
HR (95% CI)	1.00 [Reference]	1.05 (0.88-1.25)	1.13 (0.92-1.38)	1.38 (1.09-1.73)	1.11 (1.03-1.19)
Physical activity 0 min/wk					
No. of deaths	151	333	283	270	
HR (95% CI)	1.00 [Reference]	1.02 (0.84-1.24)	1.27 (1.03-1.55)	1.56 (1.26-1.92)	1.18 (1.11-1.26)
Physical activity 1-149 min/wk					
No. of deaths	289	743	358	191	
HR (95% CI)	1.00 [Reference]	1.12 (0.98-1.28)	1.24 (1.06-1.45)	1.41 (1.17-1.70)	1.12 (1.06-1.19)
Physical activity 150-299 min/wk					
No. of deaths	201	426	177	74	
HR (95% CI)	1.00 [Reference]	0.98 (0.83-1.16)	1.00 (0.82-1.23)	1.13 (0.86-1.48)	1.03 (0.95-1.11)
Physical activity ≥300 min/wk					
No. of deaths	484	987	324	114	
HR (95% CI)	1.00 [Reference]	0.96 (0.86-1.07)	1.12 (0.97-1.29)	1.57 (1.28-1.93)	1.11 (1.05-1.18)

Abbreviation: HR, hazard ratio.

[a]Australian adults 45 years or older without missing data for the relevant outcomes were included in the analysis (n = 222 497). Subgroup analyses were performed for women (n = 116 642); men (n = 105 855); groups aged 45 to 54 (n = 68 125), 55 to 64 (n = 73 825), 65 to 74 (n = 47 436), and 75 years or older (n = 33 111); participants who were considered healthy at baseline (n = 145 713) (includes those who never had cardiovascular disease, diabetes, or cancer, with the exception of nonmelanoma skin cancer); and participants with cardiovascular disease or diabetes mellitus at baseline (n = 52 229). Subgroup analyses were also performed for baseline body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) for participants who were considered healthy weight (n = 81 642) (BMI, 18.5-24.9), overweight (n = 88 197) (BMI, 25.0-29.9), and obese (n = 49 810) (BMI, 30.0-60.0) and for participants with a physical activity level of 0 (n = 12 100), 1 to 149 (n = 43 466), 150 to 299 (n = 44 824), and at least 300 min/wk (n = 122 107). Hazard ratios were adjusted 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.

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.[8,30] It has also been suggested that sedentary behavior affects carbohydrate metabolism through changes in muscle glucose transporter protein content.[8] Results from molecular biology and medical chemistry studies have suggested that physical activity and seden-

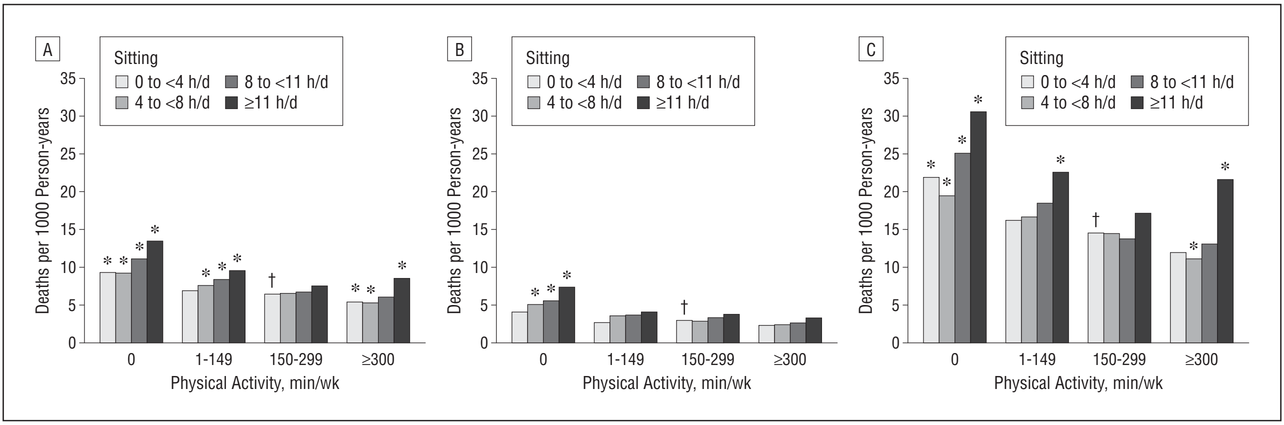

Figure. The combined relationships of sitting and physical activity with all-cause mortality. A, All participants (n = 222 497). B, Healthy participants who at baseline had no cardiovascular disease, diabetes mellitus, or cancer, with the exception of nonmelanoma skin cancer (n = 145 713). C, Participants with cardiovascular disease or diabetes at baseline (n = 52 229). Deaths per 1000 person-years were adjusted for sex, age, educational level, marital status, urban or rural residence, body mass index, smoking status, self-rated health, and receiving help with daily tasks for a long-term illness or disability. *$P<.05$ compared with the reference group. †Reference group.

tary behavior have different influences on the body, supporting their independent effects on health.[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 recommendations.[32] Furthermore, encouraging high-risk groups such as individuals with cardiovascular disease, diabetes, overweight, or obesity to sit less and be more physically active should be a public health priority.

In conclusion, prolonged sitting is a risk factor for all-cause mortality. Shorter sitting times and sufficient physical activity are independently protective against all-cause mortality not just for healthy individuals but also for those with cardiovascular disease, diabetes, overweight, or obesity.

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Correspondence: Hidde P. van der Ploeg, PhD, Level 2, Medical Foundation Building (K25), Sydney School of Public Health, University of Sydney, Sydney 2006, New South Wales, Australia (hidde.vanderploeg@sydney.edu.au).
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INVITED COMMENTARY

New Exercise Prescription

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

In their article, van der Ploeg and colleagues[1] 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 individual who does 30 minutes of brisk walking on most days of the week will have met the public health guideline on the minimum amount of activity required for health benefits. However, this still leaves some 15½ hours of nonexercise awake time each day during which, for many adults, sitting is the predominant stance. This is a consequence of the plethora of ways in which the physical, economic, and social environments have changed, particularly since the middle of the past century. These changes—in personal transportation, communication, workplace productivity, and domestic entertainment technologies—have been associated not only with decreased physical activity but also with increased time spent sitting.[3]

The findings from van der Ploeg and colleagues provide a substantial contribution to the rapidly accumulating body of evidence from observational studies identifying sedentary behavior (time spent sitting) as an important risk factor for chronic disease.[4] The authors conclude that reducing total time spent sitting as a population health risk may be at least as important as increasing participation in physical activity. To put this in perspective, 30 minutes of physical activity is as protective an exposure as 10 hours of sitting is a harmful one.[4]

The observation that prolonged sitting is hazardous to one's health is not new. A relationship between sedentary behavior and deleterious health consequences in workers was noted as early as the 17th century by occupational physician Ramazzini.[5] In the 1960s, Morris and colleagues[6] reported that workers in occupations requiring much sitting (London bus drivers and mail sorters) had higher incidences of cardiovascular disease than did workers who were required to stand and ambulate (bus conductors and postal workers). In the preceding decade, Homans[7] reported clinical cases of venous thrombosis in the legs following prolonged sitting while attending a theater performance and watching television. This led him to recommend that "such matters are important enough to suggest the advisability of making movements of the toes, feet, and lower legs when one is sitting for long periods and of getting up and exercising when opportunity offers."[7(p149)]

A possible weakness of the study by van der Ploeg and colleagues and similar cohort studies is that the main exposure variable (sitting time) is based on self-report. Newer objective-measurement capacities made possible by accelerometers—small electronic devices worn on the hip during waking hours—provide further insights. For example, examining 7 days of accelerometer data from a nationally representative sample of 1714 white adults aged 20 to 59 years from the US National Health and Nutrition Examination Survey,[3] it is striking that the vast majority of daily nonsleeping time is spent in either sedentary behavior (58%) or light-intensity activity (eg, strolling, washing dishes, and gardening) (39%) and only 3% in health-enhancing physical activity time.

Moreover, because time spent in moderate-to-vigorous physical activity is such a small component of the overall waking day, almost all the variance in sedentary time across the population is related to the extent to which the sedentary time displaces light-intensity activity.[3] Indeed, one such study[8] has reported an almost-perfect inverse correlation (−0.98) of the time spent in light-intensity activity with sedentary time. Therefore, in addition to the benefits of moderate-to-vigorous activity, health gains should accrue through redressing the imbalance between sitting time and light-intensity activity.

Besides the decreased energy metabolism of sitting compared with light-intensity activity,[9] sitting may also be harmful because of the prolonged absence of muscle contractile activity in the lower limbs. Efforts to reduce sedentary behavior will require attention to workplace regulations, occupational health and safety policy and practice, transportation planning, and innovations in the design of communication technologies, as well as public education campaigns.

With this new study, evidence is sufficiently strong that physicians should be advising patients to reduce daily sitting time. The good news is that increasing light-intensity activity may be a feasible goal for many and offers great health benefits.

David W. Dunstan, PhD
Neville Owen, PhD

Author Affiliations: Physical Activity Laboratory (Dr Dunstan) and Behavioural Epidemiology Laboratory (Dr Owen), Baker IDI Heart and Diabetes Institute, Melbourne, Australia.
Correspondence: Dr Dunstan, Physical Activity Laboratory, Baker IDI Heart and Diabetes Institute, 99 Commercial Rd, Melbourne 3003, Victoria, Australia (david.dunstan@bakeridi.edu.au).
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