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Standing time and all-cause mortality in a large cohort of Australian adults

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ABSTRACT

Objective. To determine the association between standing time and all-cause mortality.

Methods. Prospective questionnaire data from 221,240 individuals from the 45 and Up Study were linked to mortality data from the New South Wales Registry of Deaths (Australia) from February 1, 2006 to June 17, 2012. Hazard ratios for all-cause mortality according to standing time at baseline were estimated in 2013 using Cox regression modelling, adjusted for sex, age, education, urban/rural residence, physical activity, sitting time, body mass index, smoking status, self-rated health and disability.

Results. During 937,411 person years (mean follow-up = 4.2 yr) 8009 deaths occurred. All-cause mortality hazard ratios were 0.90 (95% CI 0.85–0.95), 0.85 (95% CI 0.80–0.95), and 0.76 (95% CI 0.69–0.95) for standing $2-\le 5$ h/d, $5-\le 8$ h/d, or >8 h/d respectively, compared to standing two or less hours per day. Further analyses revealed no significant interactions between standing and sex (p = 0.93), the presence/absence of cardiovascular disease or diabetes (p = 0.22), BMI (p = 0.78), physical activity (p = 0.16) and sitting time (p = 0.22).

Conclusion. This study showed a dose–response association between standing time and all-cause mortality in Australian adults aged 45 years and older. Increasing standing may hold promise for alleviating the health risks of prolonged sitting.

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Introduction

Evidence is accumulating on the detrimental health effects of prolonged sitting (Chau et al., 2013; Grontved and Hu, 2011; Proper et al., 2011; Thorpe et al., 2011; van Uffelen et al., 2010; Wilmot et al., 2012). Increasing standing has been proposed as a feasible and promising strategy to reduce sitting time (Alkhajah et al., 2012; Dunstan et al., 2012; Grunseit et al., 2013; Healy et al., 2013; Owen et al., 2011; Pronk et al., 2012). However, little is known about the long-term health implications of standing time. Recently, it was suggested that standing was associated with lower mortality risks among inactive individuals (Katzmarzyk, 2013). The objective of the current study was to determine the association between standing time and all-cause mortality in a large prospective cohort study.

Methods Study population

The analyses used data from the Sax Institute's 45 and Up Study, a large-scale prospective cohort study of men and women aged 45 years and older from the state of New South Wales (NSW), Australia. The 45 and Up Study was approved by the University of NSW Human Research Ethics Committee. The study was approved by the NSW Population and Health Services Research Ethics Committee (reference No. 2010/05/234). A detailed description of the 45 and Up Study can be found elsewhere (45 and Up Study Collaborators, 2008).

Study variables

Participants completed a baseline questionnaire (available at www. saxinstitute.org.au/our-work/45-up-study) between February 2006 and December 2009. Self-reported time spent standing was assessed with the question 'About how many hours in each 24 h day do you usually spend standing?' Sitting time was assessed with the question 'About how many hours in each 24 h day do you usually spend sitting?' Total moderate to vigorous intensity physical activity was assessed with the Active Australia Survey, which measures walking and other moderate- and vigorous-intensity physical activity







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(Australian Institute of Health and Welfare (AIHW), 2003). All-cause mortality was ascertained from the NSW Registry of Births, Deaths and Marriages for the period 1/2/2006-17/6/2012. More details on the assessments can be found elsewhere (45 and Up Study Collaborators, 2008; van der Ploeg et al., 2012).

Statistical analyses

Hazard ratios for all-cause mortality according to standing time categories $(\leq 2 \text{ h/d}, 2 \leq 5 \text{ h/d}, 5 \leq 8 \text{ h/d}, >8 \text{ h/d})$ at baseline were estimated using Cox regression modelling (Cox, 1972), in which the underlying time variable was age. Standing time categories were defined a priori and loosely based on quartiles, while still including sufficient contrast within the low-end-skewed standing distribution. Hazard ratios for standing time categories relative to the first standing time category were calculated, as well as tests for trends over the four standing categories. Cox regression analyses were adjusted for self-reported sex, age (default), education, marital status, urban/rural residence, BMI, physical activity (walking and other moderate to vigorous physical activity), daily sitting time and smoking status. To account for possible reverse causation due to existing disease, self-rated health and receiving help with daily tasks for a long term illness or disability were also adjusted for. People with missing data on standing, sitting time or physical activity or where sitting and standing time added up to more than 24 h/d were excluded from the analyses. Missing data for all other adjustment variables were included in the analyses as a separate category.

The Cox regression models were repeated for a priori defined subgroups of people with cardiovascular disease (including heart disease, stroke, thrombosis) or diabetes, and for people who were considered (relatively) healthy with no cardiovascular disease, diabetes or cancer (with the exception of non-melanoma skin cancer). Regression models were also repeated with stratifications for sex, age, BMI, physical activity and sitting time. To determine if the association between standing and all-cause mortality differed between subgroups, interaction effects were determined with a likelihood ratio test comparing the model with and without interaction term.

Finally, a sensitivity analysis with only participants who had more than 1 year of follow-up was performed to check for potential confounding of occult disease at baseline.

Results

The characteristics of the cohort participants (n = 221,240) by time spent standing are presented in Table 1. Standing time was lowest in people with age 75 years or older, a university degree, fair/poor selfrated health, requirements for help with daily tasks, lower physical activity levels and higher sitting levels.

Mean follow-up time was 4.2 (SD = 0.9) years and during 937,411 person years 8009 deaths occurred. Table 2 presents the results from

Table 1

Characteristics of the cohort participants by time spent standing.

Variable	$\frac{\text{Standing } 0 - \le 2 \text{ h/d}}{\text{No. (row \%)}}$	$\frac{\text{Standing } 2 - \le 5 \text{ h/d}}{\text{No. (row \%)}}$	$\frac{\text{Standing } 5 - \le 8 \text{ h/d}}{\text{No. (row \%)}}$	Standing >8 h/d No. (row %)	Total sample No. (column %)
Sex					
Male	35,405 (33.8)	30,883 (29.5)	24,606 (23.5)	13,880 (13.2)	104,774 (47.4)
Female	37,676 (32.3)	35,816 (30.8)	26,581 (22.8)	16,393 (14.1)	116,466 (52.6)
Age (yrs)					
45–54	22,589 (32.6)	20,115 (29.0)	15,501 (22.3)	11,190 (16.1)	69,395 (31.4)
55-64	22,711 (30.7)	22,051 (29.8)	18,037 (24.3)	11,276 (15.2)	74,075 (33.5)
65-74	14,517 (31.2)	14,646 (31.5)	11,707 (25.1)	5695 (12.2)	46,565 (21.0)
≥75	13,264 (42.5)	9887 (31.7)	5942 (19.0)	2112 (6.8)	31,205 (14.1)
Education	,,			(
Low (\leq did not complete high school)	22,000 (31.8)	20,996 (30.4)	16,508 (23.9)	9666 (14.0)	69,170 (31.6)
Middle	28,422 (30.1)	27,652 (29.3)	23,272 (24.7)	14,930 (15.8)	94,276 (43.1)
High (\geq completed university)	21,778 (39.5)	17,211 (31.2)	10,779 (19.6)	5350 (9.7)	55,118 (25.2)
Marital status	21,770 (0010)	17,211 (3112)	10,770 (1010)	0000 (017)	55,110 (2012)
Married/de facto	53,488 (31.7)	50,995 (30.2)	40,248 (23.8)	24,151 (14.3)	168,882 (76.7)
Other	19,206 (37.5)	15,385 (30.0)	10,667 (20.8)	5965 (11.6)	51,223 (23.3)
Location of residence					
Rural	18,499 (28.5)	18,962 (29.2)	16,738 (25.8)	10,639 (16.4)	64,838 (29.3)
Urban	54,565 (34.9)	47,717 (30.5)	34,440 (22.0)	19,629 (12.6)	156,351 (70.7)
BMI	,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	, (****,			
<18.5	897 (35.1)	735 (28.7)	572 (22.4)	353 (13.8)	2557 (1.2)
18.5-<25	24,207 (31.9)	22,130 (29.2)	18,154 (23.9)	11,416 (15.0)	75,907 (36.6)
25-<30	26,730 (32.4)	25,215 (30.6)	19,184 (23.3)	11,270 (13.7)	82,399 (39.8)
≥30	16,755 (36.2)	14,402 (31.1)	9932 (21.4)	5244 (11.3)	46,333 (22.4)
Smoking status					
Current smoker	4825 (30.5)	4665 (29.5)	3799 (24.0)	2541 (16.1)	15,830 (7.2)
Ex-smoker	26,391 (33.3)	23,876 (30.1)	18,525 (23.4)	10,508 (13.3)	79,300 (35.9)
Never smoked	41,669 (33.2)	37,949 (30.2)	28,712 (22.9)	17,133 (13.7)	125,463 (56.9)
Self-rated health status					
Excellent	10,478 (30.8)	9685 (28.5)	8145 (23.9)	5721 (16.8)	34,029 (15.8)
Very good	24,596 (30.1)	24,803 (30.3)	20,103 (24.6)	12,330 (15.1)	81,832 (38.0)
Good	23,653 (33.1)	22,031 (30.9)	16,555 (23.2)	9148 (12.8)	71,387 (33.2)
Fair	10,015 (41.8)	7281 (30.4)	4552 (19.0)	2102 (8.8)	23,950 (11.1)
Poor	2271 (57.6)	1049 (26.6)	423 (10.7)	200 (5.1)	3943 (1.8)
Help with daily tasks because of long term illness or disability			()		
No	64,451 (31.9)	61,193 (30.3)	47,999 (23.7)	28,577 (14.1)	202,220 (95.2)
Yes	5652 (54.9)	2824 (27.4)	1258 (12.2)	570 (5.5)	10,304 (4.8)
Moderate to vigorous intensity physical activity (min/wk)	0002 (0 110)	2021(2711)	1200 (1212)	575 (515)	10,001(110)
0	5133 (48.8)	2621 (24.9)	1709 (16.2)	1057 (10.0)	10,520 (4.8)
1–149	15,584 (41.9)	11,195 (30.1)	6812 (18.3)	3581 (9.6)	37,172 (16.8)
150–299	15,521 (38.3)	12,664 (31.2)	8235 (20.3)	4109 (10.1)	40,529 (18.3)
> = 300	36,843 (27.7)	40,219 (30.2)	34,431 (25.9)	21,526 (16.2)	133,019 (60.1)
Sitting (h/d)	30,515 (27.7)	10,210 (30,2)	5 ., 151 (25.5)	21,520 (10.2)	133,013 (00,1)
0-<4	16,756 (29.0)	13,719 (23.7)	13,039 (22.6)	14,256 (24.7)	57,770 (26.1)
4-<8	30,141 (27.9)	34,508 (31.9)	28,687 (26.5)	14,811 (13.7)	108,147 (48.9)
4-<0 8-<11	18,235 (43.8)	13,448 (32.3)	8773 (21.1)	1206 (2.9)	41,662 (18.8)
≥11	7949 (58.2)	5024 (36.8)	688 (5.0)	Excluded	13,661 (6.2)

Table 2

Association between standing and all-cause mortality among Australian adults aged \geq 45 years.^a

Population	Standing 0–≤2 h/d	Standing 2–≤5 h/d	Standing 5-≤8 h/d	Standing >8 h/d	Trend
All participants					
No. of deaths	3864	2286	1340	519	
Hazard ratio (95%CI)	1.00 [Reference]	0.90 (0.85-0.95)	0.85 (0.80-0.95)	0.76 (0.69-0.95)	0.92 (0.90-0.94)
Women					
No. of deaths	1442	827	417	176	
Hazard ratio (95%CI)	1.00 [Reference]	0.92 (0.84–1.00)	0.86 (0.76-0.96)	0.79 (0.67–0.93)	0.92 (0.89-0.97)
Men	2 422	1.450	000	2.42	
No. of deaths	2422	1459	923	343	
Hazard ratio (95%CI)	1.00 [Reference]	0.88 (0.82-0.94)	0.84 (0.78–0.91)	0.74 (0.66-0.83)	0.91 (0.88-0.94)
Age 45–54 years No. of deaths	189	138	96	48	
Hazard ratio (95%CI)	1.00 [Reference]	0.91 (0.72–1.13)	96 0.88 (0.68–1.14)	48 0.64 (0.45–0.90)	0.89 (0.81-0.98)
Age 55–64 years	1.00 [Reference]	0.51 (0.72-1.15)	0.00 (0.00-1.14)	0.04 (0.45-0.50)	0.03 (0.01-0.30)
No. of deaths	402	336	225	113	
Hazard ratio (95%CI)	1.00 [Reference]	0.99 (0.86–1.15)	0.89 (0.75–1.05)	0.78 (0.63-0.98)	0.93 (0.87-0.99)
Age 65–74 years	noo [nerenee]	0.00 (0.00 1110)			
No. of deaths	761	525	348	151	
Hazard ratio (95%CI)	1.00 [Reference]	0.84 (0.75-0.95)	0.77 (0.67-0.88)	0.76 (0.63-0.91)	0.90 (0.85-0.94)
Age \geq 75 years		, ,	. ,	. ,	. , ,
No. of deaths	2512	1287	671	207	
Hazard ratio (95%CI)	1.00 [Reference]	0.89 (0.83-0.95)	0.89 (0.81-0.97)	0.82 (0.71-0.95)	0.93 (0.90-0.97)
Healthy					
No. of deaths	1056	701	468	193	
Hazard ratio (95%CI)	1.00 [Reference]	0.94 (0.85-1.03)	0.93 (0.83-1.04)	0.80 (0.68-0.94)	0.94 (0.90-0.99)
Cardiovascular disease or diabetes					
No. of deaths	2102	1143	564	214	
Hazard ratio (95%CI)	1.00 [Reference]	0.90 (0.84-0.97)	0.81 (0.73-0.89)	0.82 (0.71-0.94)	0.92 (0.88-0.95)
Normal weight	1501	200	F1C	210	
No. of deaths	1501 1.00 [Reference]	890 0.90 (0.83–0.99)	516 0.83 (0.75–0.92)	219 0.78 (0.67–0.90)	0.92 (0.88-0.95)
Hazard ratio (95%CI) Overweight	1.00 [Reference]	0.90 (0.85-0.99)	0.85 (0.75-0.92)	0.78 (0.07-0.90)	0.92 (0.88-0.95)
No. of deaths	1.00 [Reference]	769	445	177	
Hazard ratio (95%CI)	1.00 [Reference]	0.91 (0.83–1.00)	0.84 (0.75–0.94)	0.79 (0.67–0.94)	0.92 (0.88-0.96)
Obese	1.00 [Reference]	0.51 (0.05 1.00)	0.01(0.75 0.51)	0.75 (0.07 0.51)	0.52 (0.00 0.50)
No. of deaths	703	378	224	76	
Hazard ratio (95%CI)	1.00 [Reference]	0.88 (0.77-1.00)	0.93 (0.79-1.09)	0.73 (0.57-0.93)	0.93 (0.87-0.99)
Moderate to vigorous intensity physical activity 0 min/wk	. ,	· · · ·		· · · ·	· · · · ·
No. of deaths	905	224	92	29	
Hazard ratio (95%CI)	1.00 [Reference]	0.78 (0.67-0.91)	0.79 (0.63-0.99)	0.55 (0.37-0.80)	0.84 (0.77-0.91)
Moderate to vigorous intensity physical activity 1–149 min/wk					
No. of deaths	1231	570	265	91	
Hazard ratio (95%CI)	1.00 [Reference]	0.86 (0.78–0.95)	0.83 (0.73-0.96)	0.77 (0.62-0.96)	0.91 (0.86-0.96)
Moderate to vigorous intensity physical activity 150–299 min/wk					
No. of deaths	623	400	177	72	
Hazard ratio (95%CI)	1.00 [Reference]	0.88 (0.78-1.00)	0.71 (0.60-0.84)	0.79 (0.62–1.01)	0.88 (0.83-0.94)
Moderate to vigorous intensity physical activity \geq 300 min/wk	1105	1002	900	227	
No. of deaths	1105	1092 0.98 (0.90–1.06)	806	327 0.83 (0.73–0.94)	
Hazard ratio (95%CI) Sitting 0–<4 h/d	1.00 [Reference]	0.98 (0.90-1.00)	0.95 (0.87–1.05)	0.65 (0.75-0.94)	0.95 (0.92–0.99)
No. of deaths	854	371	275	214	
Hazard ratio (95%CI)	1.00 [Reference]	0.80 (0.71–0.91)	0.87 (0.75–1.00)	0.76 (0.65–0.89)	0.92 (0.87-0.96)
Sitting 4–<8 h/d	1.00 [Reference]	0.00 (0.71-0.51)	0.07 (0.75-1.00)	0.70 (0.05-0.85)	0.32 (0.87-0.30)
No. of deaths	1555	1229	812	269	
Hazard ratio (95%CI)	1.00 [Reference]	0.89 (0.83-0.96)	0.86 (0.78-0.94)	0.75 (0.65-0.85)	0.92 (0.88-0.95)
Sitting 8–<11 h/d				. ((
No. of deaths	876	509	227	36	
Hazard ratio (95%CI)	1.00 [Reference]	1.03 (0.92-1.15)	0.85 (0.73-0.99)	0.92 (0.65-1.28)	0.92 (0.65-1.28)
Sitting $\geq 11 \text{ h/d}$. ,	. ,	. ,	. ,	. ,
No. of deaths	579	177	26		
Hazard ratio (95%CI)	1.00 [Reference]	0.85 (0.71-1.02)	0.89 (0.59–1.33)	Excluded	0.89 (0.77-1.03)

^a Australian adults (age \geq 45) without missing data for the relevant outcomes were included in the analysis (n = 221,240). Subgroup analyses were done for women (n = 116,466), men (n = 104,774), age 45–54 (n = 69,395), 55–64 (n = 74,075), 65–74 (n = 46,565), and \geq 75 (n = 31,205), people who were considered healthy at baseline (n = 145,984; who never had cardiovascular disease, diabetes or cancer (with the exception of non-melanoma skin cancer)) and for people with cardiovascular disease or diabetes at baseline (n = 50,967). Subgroup analyses were also performed for baseline body mass index (BMI) for people who were considered healthy weight (n = 75,907; BMI 18.5–24.9 kg/m²), overweight (n = 82,399; BMI 25.0–29.9 kg/m²), and obese (n = 46,333; BMI 30–60 kg/m²); for moderate to vigorous intensity physical activity level 0 min/wk (n = 10,520), 1–149 min/wk (n = 37,172), 150–299 min/wk (n = 40,529), and \geq 300 min/wk (n = 133,019); and for sitting time 0–<4 h/d (n = 57,770); 4–<8 h/d (n = 108,147); 8–<11 h/d (n = 141,662); \geq 11 h/d (n = 13,661). Hazard ratios were adjusted for sex, age, education, marital status, urban or rural residence, moderate to vigorous intensity physical activity, sitting time, BMI, smoking status, self-rated health, and receiving help with daily tasks for a long term illness or disability.

the adjusted Cox proportional-hazards regression analyses on the relationship between standing and all-cause mortality. Hazard ratios were 0.90 (95% CI 0.85–0.95), 0.85 (95% CI 0.80–0.95), 0.76 (95% CI 0.69–0.95) for standing $2-\le 5$ h/d, $5-\le 8$ h/d, or >8 h/d respectively,

compared to standing two or less hours per day. Sensitivity analyses excluding people who died in the first year of follow-up (n = 220,497) revealed similar hazard ratios of 0.90 (0.85–0.95), 0.87 (0.81–0.93), 0.78 (0.71–0.86), respectively. Similarly, excluding those with prevalent

cardiovascular disease, diabetes and cancer at baseline attenuated the observed associations only slightly (Table 2). All other stratified analyses presented in Table 2 revealed few differences in the relationship between standing and all-cause mortality across different strata. Moreover, further exploration of the subgroups revealed no significant interaction effects between standing and sex (p = 0.93), the presence/absence of cardiovascular disease or diabetes (p = 0.22), BMI (p = 0.78), physical activity (p = 0.16) and sitting time (p = 0.22). The relationship between standing and all-cause mortality for different sitting time categories was similar but became non-significant for the two highest sitting time categories. As this is likely due to statistical power issues (few report high sitting and high standing time), we performed a sensitivity analysis combining the two groups, which showed that the hazard ratio for the trend of those sitting ≥ 8 h/d was 0.92 (0.87–0.98).

Discussion

This study showed a significant association between standing time and all-cause mortality in Australian adults aged 45 years and older after adjustment for covariates. This association was consistent across sex, age, BMI, moderate to vigorous intensity physical activity and sitting time subgroups and was independent of health status.

The findings of this study expand on the recent Canadian data, which also showed a dose-response association between standing and allcause mortality as well as associations with cardiovascular mortality and non-cardiovascular/non-cancer mortality (Katzmarzyk, 2013). The current study had a substantially larger sample size, and adjusted for health status. The Canadian study also revealed an interaction between physical activity and standing, and the association between standing and mortality was significant only among the physically inactive (<7.5 MET.h.wk⁻¹) (Katzmarzyk, 2013). The current study also suggests that the association between standing and all-cause mortality was somewhat stronger among the least physically active participants. The most physically active category (\geq 300 min/wk) showed only people standing more than 8 h/d had a significantly lower all-cause mortality risk than people standing 2 h/d or less. However, unlike the Canadian study the interaction between standing and physical activity was not significant in the current study.

Interestingly, the Spearmans Rho correlation between sitting and standing was -0.233 (p < 0.0001), suggesting standing time is not the inverse of sitting time. This was also argued by Katzmarzyk, who reported a correlation of -0.52 (p < 0.0001) (Katzmarzyk, 2013).

The limitations of this study include the possibility of unmeasured confounding and confounding due to occult disease. However, analyses were adjusted for many potential confounders and our sensitivity analyses, which excluded people who died in the first year and people who had established chronic disease at baseline, showed similar results. Nevertheless, excluding only the first year of follow up can be considered as somewhat minimal, but the relatively short follow up of the study precluded the exclusion of more years. Another limitation is that little is known about the measurement properties of the standing question. It is possible that participants interpret the standing question as being on their feet, which might than include some light intensity walking or other activities as well. However, the low correlation between sitting and standing time suggested that standing time was at least not interpreted as all light intensity activity, which is generally considered the inverse of sitting time. Furthermore, a similarly simple occupational standing question showed acceptable measurement properties (Chau et al., 2012). Nonetheless, future studies would benefit from objective assessments of the full activity spectrum, including sedentary time, standing time, time spent in other light intensity activities, and moderate and vigorous physical activity. These objective assessments are still likely to benefit from self-report measures that give more domain specific information, such as a diary for recording working hours or more general time use diaries (Gomersall et al., 2011; van der Ploeg et al., 2010).

In conclusion, standing was beneficially associated with all-cause mortality independent of siting, moderate to vigorous intensity physical activity and health status. Assuming the observed associations are causal, increasing standing may have health benefits for people who sit for a considerable part of the day. It must be noted that prolonged standing can increase the risk on musculoskeletal problems and varicose veins (Halim et al., 2012; Tuchsen et al., 2005), and hence should be alternated with periods of sitting and physical activity.

Conflict of interest

The authors declare that there are no conflicts of interest.

Acknowledgments

This research was completed using data collected through the 45 and Up Study (www.saxinstitute.org.au). The 45 and Up Study is managed by the Sax Institute in collaboration with major partner Cancer Council NSW; and partners: the National Heart Foundation of Australia (NSW Division); NSW Ministry of Health; *beyondblue*; Ageing, Disability and Home Care, Department of Family and Community Services; the Australian Red Cross Blood Service; and UnitingCare Ageing. We thank the many thousands of people participating in the 45 and Up Study. These analyses were supported by Australian National Health and Medical Research Council Program Grant #301200. ES was also supported by a Career Development Fellowship by the National Institute for Health Research (UK) (CDF-2010-03-30). The views expressed here are of the authors and not necessarily of the funding bodies.

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