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Occupational sitting time and subsequent risk of cancer: The Japan Public Health Center-based Prospective Study

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Abstract

Although occupational sitting time has been associated with adverse health outcomes and mortality, the association with cancer incidence remains unknown. This study investigated the association between occupational sitting time and risk of total and site-specific cancer in a Japanese population. We evaluated 33 307 participants aged 50-79 years who responded to a questionnaire in 2000-2003 in the Japan Public Health Center-based Prospective Study and were followed until 2013. Participants were grouped by sitting time at work. Hazard ratio (HR) and 95% confidence interval (CI) of cancer incidence were calculated with adjustment for potential confounders including moderate-to-vigorous physical activity. During 10.2 years of follow-up, 3807 newly diagnosed cases of cancer were identified. Occupational sitting time was marginally associated with total cancer, with multivariable HRs for the ≥7 h/d vs 1 to <3 h/d category of 1.12 (95% CI, 0.99-1.26; P for trend = .071) in men, but not women. Among findings for cancers at specific sites, long occupational sitting time was associated with increased risk of pancreas cancer, with multivariable HRs for the ≥7 h/d vs 1 to <3 h/d category of 2.25 (95% CI, 1.17-4.34; P for trend = .021) in men, and lung cancer, with multivariable HRs for the ≥7 h/d vs 1 to <3 h/d category of 2.80 (95% CI, 1.33-5.90; P for trend = .013) in women. Extended sitting time at work was associated with an increased risk of pancreas cancer in men and lung cancer in women.

KEYWORDS
cancer incidence, Japan Public Health Center-based Prospective Study, leisure-time physical activity, sedentary behavior, sitting time

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1 | INTRODUCTION

Sedentary behavior is any waking behavior characterized by an energy expenditure less than or equal to 1.5 metabolic equivalents, while in a sitting, reclining, or lying posture.[1] Particularly, long sitting time at work is suggested to be an important risk factor for a number of adverse health outcomes, including diabetes mellitus,[2] some cancers,[3] and mortality,[2,4,5] independent of MVPA. In a recent meta-analysis of 21 cohort and 22 case-control studies, the author reported an association between occupational sitting time and an increased risk of colon cancer.[3] However, evidence on the association between occupational sitting time and cancer risk at other sites is not consistent. Additionally, despite differences in working time across countries,[6] few studies[7,8] have reported the putative association between occupational sitting time and cancer incidence in an Asian population, including Japan. Given that sampling from a diverse group of 20 countries identified Japanese as having the longest total sitting time[9] and that approximately 65% of total sitting time on workdays was spent sitting at work in both men and women,[10] it is important to evaluate the association between occupational sitting time and risk of cancer incidence in Japanese populations. Furthermore, it is also unknown whether high levels of physical activity in leisure time eliminate any cancer risk by long sitting time at work.

Here, we examined the association between occupational sitting time and the risk of total and site-specific cancer in a large Japanese population.

2 | MATERIALS AND METHODS

2.1 | Study cohort

The Japan Public Health Center-based Prospective study consists of 2 cohorts, cohort I and cohort II, which started in 1990 and 1993, respectively. Cohort I included residents aged 40-59 years in 5 Japanese PHC areas (Iwate, Akita, Nagano, Okinawa, and Tokyo), and cohort II included residents aged 40 to 69 years in 6 PHC areas (Ibaraki, Niigata, Kochi, Nagasaki, Okinawa, and Osaka). Details of the study design have been reported previously.[11] This study consisted of baseline, as well as 5-year (second) and 10-year (third) follow-up surveys. Study participants were informed of the aims of the study, and those who completed the survey questionnaire were regarded as consenting to participation. The study was approved by the Institutional Review Board of the National Cancer Center, Tokyo, Japan.

At baseline survey, 140 420 individuals were identified as constituting the study population. In the present analysis, we excluded Tokyo participants from the analyses because data on cancer incidence were not available. In this study, the 10-year follow-up survey undertaken in 2000-2003 was defined as a starting point, because that survey included more comprehensive information on occupational sitting time than the baseline or 5-year follow-up survey. Participants aged 50-79 years were followed until 2013. The questionnaire was used to collect information on the medical history and lifestyle variables of the participants. After excluding 27 612 participants who were ineligible (non-Japanese nationality, incorrect late report of migration occurring before the starting point, or incorrect birth data) or had died, moved out of the study area, or were lost to follow-up before the starting point, 112 808 participants were eligible for participation. Of these, a total of 93 813 participants responded to the 10-year follow-up questionnaire (response rate 83.2%).

2.2 | Occupational sitting time and physical activity in leisure time

The main exposure variable, occupational sitting time, was assessed with the question "How long do you spend in the following tasks at work?", as in a previous study.[4] Participants were asked to report the average duration for each of "sitting tasks", "standing tasks", "walking tasks", and "strenuous tasks" using the following options: (i) none; (ii) 0 to <1; (iii) 1 to <3; (iv) 3 to <5; (v) 5 to <7; (vi) 7 to <9; (vii) 9 to <11; and (viii) ≥11 hours/day. Occupational sitting time was then categorized into 5 groups: short, <1 hours/day; 1 to <3 hours/day; 3 to <5 hours/day; 5 to <7 hours/day; or longer, ≥7 hours/day.

We assessed MVPA time in leisure time as covariates and to undertake subgroup analyses. Participants were asked "How often do you engage in the following activities in your leisure time?" with the following possible answers: (i) walking slowly; (ii) brisk walking; (iii) moderate-intensity activity, such as playing golf or gardening; and (iv) vigorous intensity activity, such as jogging or playing tennis. They were then asked the frequency options of: (i) <1 time/month; (ii) 1-3 times/month; (iii) 1-2 times/week; (iv) 3-4 times/week; and (v) almost every day; and the duration options (time/session) of: (i) <30 minutes; (ii) 30 to <59 minutes; (iii) 1 to <2 hours; (iv) 2 to <3 hours; (v) 3 to <4 hours; and (vi) ≥4 hours. We defined "brisk walking", "moderate-intensity activity", and "vigorous intensity activity" as MVPA in leisure time.[12] The average time of MVPA (minutes/week) in leisure time was determined by multiplying frequency and duration.

2.3 | Follow-up and identification of cancer cases

All participants in this study were followed from the starting point until 31 December 2013, except for one PHC area, where follow-up was until the end of 2012. Cancer incidence was identified by active cancer patient notification through the major local hospitals in the study area and by data linkage with population-based cancer registries. During the follow-up period, 13 612 (14.5%) participants died, 3983 (4.2%) moved out of the study area, and 53 (0.1%) were lost to follow-up. Cancer sites were coded according to the International Classification of Diseases for Oncology, Third Edition. The proportion of total cancer cases ascertained by death certificate only was 4.2%, which was considered satisfactory for the present study. If multiple cancers had been diagnosed at different times, the earliest cancer diagnosis date was used in this analysis.

2.4 | Statistical analysis

Of the 93 813 participants who responded to the 10-year follow-up questionnaire, 6734 aged 75 years and older, 2914 with a history of cancer, 4407 with a history of cardiovascular disease, 1481 with moderate or severe physical limitation, and 3331 with missing information for any variable used in the present analysis were excluded. Furthermore, with regard to occupation, 6711 men (18.8%) and 6497 women (15.3%) who were not presently employed, 43 men and 16 740 women who were working in home duties, 5130 who worked for at least 3 hours daily, and 6518 who had changed jobs within the last 5 years were also excluded. Finally, 33 307 participants (20 030 men and 13 277 women) were eligible for analysis. Person-years of follow-up were calculated for each subject from the starting point until the date of cancer diagnosis, date of migration from a study to a nonstudy area, date of death, or to the end of follow-up, whichever occurred first.

Participant characteristics at the starting point were compared by analysis of variance or Kruskal-Wallis tests. Hazard ratios and 95% CI between occupational sitting time and cancer risks were calculated using Cox proportional hazard regression models. All analyses were done using SAS version 9.3 (SAS Institute, Cary, NC, USA).

The basic models were adjusted for age (continuous) and area (10 PHCs). Multivariate models included related covariates such as history of diabetes (no, yes), smoking status (never, former, or current), alcohol intake status (nondrinker or occasional drinker, 1-150 g/week or ≥150 g/week), BMI (<18.5, 18.5-24.9, 25-29, or ≥30), coffee intake (almost none, 1-4 times/week, 1-2 cups/day, or ≥3 cups/day), walking task time at work (continuous), strenuous task time at work (continuous), MVPA time in leisure time (continuous), type of job (primary industry, or secondary or tertiary industry) and total working hours (continuous). We added a covariate for age at menopause (<44, 45-49, ≥50 years, or unknown) to examine associations between occupational sitting time and breast, ovary, and endometrial cancer. Subgroup analyses were undertaken by BMI (<25 or ≥25) and MVPA time in leisure time (<30 minutes/week or ≥30 minutes/week). To avoid potential bias arising from the fact that physical activity declines early in the course of cancer, analyses were repeated after excluding cancer cases diagnosed within the first 3 years of follow-up. We also undertook sensitivity analyses that were limited to the full-time workers (≥7 hours/day). We tested for linear trends by assignment of ordinal value categories of occupational sitting time. Furthermore, we calculated P interaction values by a likelihood-ratio test to compare Cox proportional hazards models with and without cross-product terms for occupational siting time (<3 hours or ≥3 hours) and BMI (<25 or ≥25) and MVPA time in leisure time (<30 minutes/week or ≥30 minutes/week). All statistical tests reported were 2-sided, and differences were considered significant at P < .05.

3 | RESULTS

During 373 809 person-years of follow-up (average follow-up, 10.2 years) for 33 307 participants, a total of 3807 cancer cases

were newly diagnosed and included in the analyses. Participant characteristics at starting points according to occupational sitting time are shown in Table 1. Participants with long occupational sitting time were younger, had greater BMI (men only), higher coffee intake, higher prevalence of diabetes (men only), shorter walking time at work, shorter strenuous time at work and undertook longer MVPA time in leisure time (men only).

Table 2 shows age- and area-adjusted and multivariable HRs and 95% CIs for total and site-specific cancer according to occupational sitting time in men. Occupational sitting time was marginally associated with the risk of total cancer, with multivariable HRs for the ≥7 h vs 1 to <3 h category of 1.12 (95% CI = 0.99-1.26, P for trend = 0.071). Furthermore, long sitting time at work was significantly associated with an increased risk of pancreas cancer, with multivariable HRs for the ≥7 h vs 1 to <3 h category of 2.25 (95% CI = 1.17-4.34, P for trend = 0.021) (Table 2).

In women, we observed no association between occupational sitting time and risk of total cancer, with multivariable HRs for the ≥7 h vs 1 to <3 h category of 1.08 (95% CI = 0.87-1.33, P for trend = 0.562) (Table 3). We found that long sitting time at work was significantly associated with an increased risk of lung cancer, with multivariable HRs for the ≥7 h vs 1 to <3 h category of 2.80 (95% CI = 1.33-5.90, P for trend = 0.013) (Table 3).

No association between extremely short occupational sitting time and total or any site-specific cancer was observed in men (Table 2) or women (Table 3), except for lung cancer in women.

Table 4 shows multivariable HRs and 95% CIs for total and pancreas cancer by BMI and MVPA time in leisure time in men. Regarding BMI, we observed a positive association between occupational sitting time and risk of pancreas cancer in men who had low BMI, with multivariable HRs for the <3 h vs ≥3 h category of 1.83 (95% CI = 1.07-3.13). In contrast, no association was shown between occupational sitting time and pancreas cancer risk in men who had high BMI. However, we did not detect statistically significant interactions between occupational sitting time and BMI for pancreas cancer. Additionally, regarding MVPA time in leisure time, we did not observe statistically significantly associations between occupational sitting time and any cancer risk in men who had a short or long MVPA time in leisure time.

There were no substantial differences in results on the inclusion of participants who worked in home duties in women (Table S1) with and without adjustment for BMI (data not shown). Sensitivity analyses after excluding participants with a cancer diagnosis within the first 3-year follow-up period or without full-time work showed no substantial differences in findings (data not shown).

4 | DISCUSSION

In this study, we found that long time spent sitting at work showed statistically significant associations with an increased risk of pancreas cancer in men and lung cancer in women. Furthermore, we also found a marginally positive association between long occupational sitting time and total cancer risk in men. These findings are consistent

TABLE 1 Baseline characteristics of study participants according to daily occupational sitting time

	Occupational sitting time (h)					
	<1	1 to <3	3 to <5	5 to <7	≥7	P value
Men (n = 20 030)						
No. of subjects	5410	5140	3267	2597	3616	
Age (y), mean ± SD	58.6 ± 6.4	58.4 ± 6.4	58.0 ± 6.3	57.5 ± 5.9	56.8 ± 5.4	<.001
BMI, mean ± SD	23.6 ± 2.9	23.8 ± 2.9	24.0 ± 2.9	24.1 ± 2.9	24.0 ± 2.9	<.001
Current smoker, %	43.9	44.0	43.7	42.8	43.7	.603
Alcohol intake (≥150 ethanol g/wk), %	54.2	54.4	52.2	51.9	52.9	.044
Coffee intake (daily), %	28.8	33.7	40.6	43.0	40.9	<.001
Diabetes, %	6.4	7.6	7.2	8.1	9.0	<.001
Walking time at work (h/d), mean ± SD	3.1 ± 2.9	2.9 ± 2.5	2.1 ± 2.1	1.6 ± 1.8	2.0 ± 2.7	<.001
Strenuous time at work (h/d), mean ± SD	3.3 ± 2.9	2.7 ± 2.5	1.7 ± 2.2	1.2 ± 1.9	1.6 ± 2.6	<.001
MVPA time in leisure time (min/wk), mean ± SD	111.1 ± 251.6	135.4 ± 263.0	154.2 ± 265.9	155.1 ± 256.7	146.3 ± 269.0	<.001
Type of job						
Primary industry, %	28.0	23.1	16.7	10.9	9.1	<.001
Secondary or tertiary industry, %	72.0	76.9	83.3	89.0	90.9	
Total working hours, mean ± SD	7.8 ± 1.8	8.0 ± 2.0	8.0 ± 2.1	8.3 ± 1.9	9.1 ± 1.7	<.001
Women (n = 13 277)						
No. of subjects	3305	3800	2435	1634	2103	
Age (y), mean ± SD	58.4 ± 6.2	58.3 ± 6.3	58.2 ± 6.2	57.3 ± 6.1	56.5 ± 5.4	.058
BMI, mean ± SD	23.5 ± 3.2	23.6 ± 3.1	23.7 ± 3.2	23.5 ± 3.3	23.6 ± 3.2	.105
Current smoker, %	5.4	5.9	6.1	5.8	5.4	.966
Alcohol intake (≥150 ethanol g/wk), %	5.1	5.2	5.6	5.1	5.0	.981
Coffee intake (daily), %	42.5	45.2	45.4	48.7	49.7	<.001
Diabetes, %	3.0	3.5	3.4	3.1	3.1	.972
Walking time at work (h/d), mean ± SD	3.7 ± 3.2	3.4 ± 2.8	2.9 ± 2.5	2.2 ± 2.1	2.5 ± 2.8	<.001
Strenuous time at work (h/d), mean ± SD	2.3 ± 2.7	1.9 ± 2.4	1.3 ± 2.0	1.0 ± 1.8	1.3 ± 2.4	<.001
MVPA time in leisure time (min/wk), mean ± SD	113.8 ± 248.9	131.2 ± 258.7	141.6 ± 288.3	127.2 ± 233.4	116.3 ± 240.3	.048
Age at menopause (≥50 y), %	47.7	48.6	47.2	46.9	47.0	<.001
Type of job						
Primary industry, %	29.2	25.8	20.4	16.6	13.8	<.001
Secondary or tertiary industry, %	70.8	74.2	79.6	83.4	86.2	
Total working hours, mean ± SD	7.9 ± 2.3	7.9 ± 2.4	7.7 ± 2.4	8.1 ± 2.2	9.0 ± 1.9	<.001

Abbreviations: BMI, body mass index; MVPA, moderate-to-vigorous physical activity.

with a guideline on physical activity that states that people should minimize the amount of time spent sitting.[13,14] It is becoming more important to reduce sitting time at work, because approximately 65% of total sitting time on workdays is spent sitting at work in both men and women[10] and because desk workers and other sedentary occupations have increased in recent years.[15] The findings of this study provided evidence that reducing occupational sitting time is also important from the perspective of cancer prevention.

Regarding pancreas cancer, 1 cohort study showed an association between sedentary work and increased risk of pancreas cancer in Finnish women,[16] but not in men. To our knowledge, this is the first large cohort study to report a positive association between occupational sitting time and pancreas cancer risk in men. Our results in men support the previous finding in women,[16] albeit that the interpretation of our result requires caution due to the small number of cases.

Several biological mechanisms to explain the observed positive association between sedentary behavior and cancer have been proposed, including adiposity, metabolic dysfunction, and chronic inflammation.[17,18] Previous experimental studies have also

TABLE 2 Hazard ratios for cancer incidence at total and specific sites according to daily occupational sitting time in men

| | Occupational sitting time (h) | | | | | |
| | <1 | 1 to <3 | 3 to <5 | 5 to <7 | ≥7 | P for trend[a] |
	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)	HR (95% CI)	
Men						
Total						
Number of subjects	5410	5140	3267	2597	3616	
Person-years	60 402	56 687	35 600	28 125	39 954	
Number of cases	788	728	479	347	500	
Age- and area-adjusted HR	1.02 (0.92-1.13)	1.00 (ref)	1.08 (0.97-1.22)	1.03 (0.91-1.17)	1.13 (1.00-1.26)	.080
Multivariable HR	1.03 (0.93-1.14)	1.00 (ref)	1.08 (0.96-1.21)	1.03 (0.90-1.17)	1.12 (0.99-1.26)	.071
Esophagus						
Number of cases	30	30	12	8	20	
Age- and area-adjusted HR	0.96 (0.58-1.59)	1.00 (ref)	0.65 (0.33-1.27)	0.55 (0.25-1.20)	1.02 (0.58-1.80)	.856
Multivariable HR	0.92 (0.55-1.53)	1.00 (ref)	0.72 (0.37-1.42)	0.65 (0.29-1.43)	1.05 (0.58-1.87)	.924
Stomach						
Number of cases	155	144	94	68	91	
Age- and area-adjusted HR	1.00 (0.80-1.25)	1.00 (ref)	1.09 (0.84-1.41)	1.02 (0.76-1.36)	1.02 (0.78-1.33)	.945
Multivariable HR	0.99 (0.79-1.25)	1.00 (ref)	1.09 (0.84-1.41)	1.04 (0.78-1.40)	1.08 (0.82-1.41)	.568
Colorectal						
Number of cases	134	135	107	68	111	
Age- and area-adjusted HR	0.96 (0.75-1.22)	1.00 (ref)	1.28 (0.99-1.65)	1.06 (0.79-1.41)	1.26 (0.98-1.62)	.137
Multivariable HR	0.99 (0.78-1.25)	1.00 (ref)	1.26 (0.98-1.64)	1.02 (0.76-1.37)	1.17 (0.91-1.52)	.319
Colon						
Number of cases	76	87	76	50	73	
Age- and area-adjusted HR	0.85 (0.62-1.16)	1.00 (ref)	1.41 (1.03-1.92)	1.20 (0.85-1.71)	1.29 (0.94-1.77)	.149
Multivariable HR	0.89 (0.65-1.21)	1.00 (ref)	1.37 (1.00-1.87)	1.13 (0.79-1.61)	1.19 (0.87-1.65)	.356
Rectum						
Number of cases	58	48	31	18	38	
Age- and area-adjusted HR	1.15 (0.78-1.68)	1.00 (ref)	1.04 (0.66-1.64)	0.79 (0.46-1.36)	1.21 (0.79-1.85)	.597
Multivariable HR	1.18 (0.80-1.73)	1.00 (ref)	1.07 (0.68-1.68)	0.80 (0.46-1.39)	1.13 (0.73-1.75)	.697
Liver						
Number of cases	29	34	25	16	30	
Age- and area-adjusted HR	0.84 (0.51-1.38)	1.00 (ref)	1.16 (0.69-1.95)	0.97 (0.53-1.76)	1.39 (0.85-2.28)	.273
Multivariable HR	0.84 (0.51-1.39)	1.00 (ref)	1.18 (0.70-1.98)	1.00 (0.54-1.83)	1.54 (0.92-2.58)	.159
Pancreas						
Number of cases	20	16	14	13	23	
Age- and area-adjusted HR	1.18 (0.61-2.29)	1.00 (ref)	1.48 (0.72-3.03)	1.76 (0.85-3.67)	2.33 (1.23-4.44)	.008
Multivariable HR	1.17 (0.61-2.28)	1.00 (ref)	1.53 (0.74-3.16)	1.82 (0.86-3.84)	2.25 (1.17-4.34)	.021
Lung						
Number of cases	109	89	69	47	55	
Age- and area-adjusted HR	1.14 (0.86-1.51)	1.00 (ref)	1.29 (0.94-1.77)	1.17 (0.82-1.66)	1.06 (0.76-1.49)	.849
Multivariable HR	1.12 (0.84-1.48)	1.00 (ref)	1.30 (0.94-1.79)	1.17 (0.82-1.68)	1.07 (0.75-1.51)	.685
Kidney						
Number of cases	20	14	10	4	9	
Age- and area-adjusted HR	1.35 (0.68-2.69)	1.00 (ref)	1.13 (0.50-2.55)	0.60 (0.20-1.82)	1.00 (0.43-2.31)	.783

(Continues)

TABLE 2 (Continued)

	Occupational sitting time (h)					
	<1	1 to <3	3 to <5	5 to <7	≥7	P for trend[a]
	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)	HR (95% CI)	
Multivariable HR	1.35 (0.68-2.69)	1.00 (ref)	1.11 (0.49-2.51)	0.59 (0.19-1.81)	1.04 (0.44-2.47)	.731
Bladder						
Number of cases	28	31	12	12	10	
Age- and area-adjusted HR	0.88 (0.52-1.47)	1.00 (ref)	0.64 (0.33-1.26)	0.86 (0.44-1.67)	0.55 (0.27-1.13)	.121
Multivariable HR	0.86 (0.51-1.44)	1.00 (ref)	0.68 (0.34-1.33)	0.92 (0.46-1.82)	0.56 (0.27-1.17)	.188
Prostate						
Number of cases	158	137	78	57	91	
Age- and area-adjusted HR	1.06 (0.84-1.34)	1.00 (ref)	0.95 (0.72-1.26)	0.93 (0.68-1.26)	1.17 (0.90-1.53)	.327
Multivariable HR	1.09 (0.86-1.37)	1.00 (ref)	0.92 (0.70-1.22)	0.89 (0.65-1.22)	1.10 (0.84-1.45)	.543
Other						
Number of cases	108	102	68	62	65	
Age- and area-adjusted HR	1.00 (0.76-1.31)	1.00 (ref)	1.09 (0.80-1.49)	1.31 (0.96-1.80)	1.04 (0.76-1.43)	.497
Multivariable HR	1.02 (0.77-1.33)	1.00 (ref)	1.07 (0.79-1.47)	1.29 (0.93-1.78)	1.01 (0.73-1.39)	.550

Note: Multivariable hazard ratio (HR) adjusted for age (continuous), area (10 public health center areas), history of diabetes (no, yes), smoking status (never, former, or current), alcohol intake status (nondrinker or occasional drinker, 1 to <150 g/wk, or ≥150 g/wk), body mass index (<18.5, 18.5-24.9, 25-29, or ≥30), coffee (almost none, 1-4 times/wk, 1-2 cups/d, or ≥3 cups/d), walking time at work (continuous), strenuous time at work (continuous), moderate-to-vigorous physical activity time in leisure time (continuous), type of job (primary industry, or secondary or tertiary industry) and total working hours (continuous).

Abbreviations: CI, confidence interval; ref, reference.

[a]P for trend was tested by assignment of ordinal values into 4 groups (1 to <3 h, 3 to <5 h, 5 to <7 h, and ≥7 h/d).

indicated that longer sedentary time promotes higher levels of insulin and leads to the development of insulin resistance,[19,20] because skeletal muscle plays an important role in uptake of glucose in blood, and even light-intensity physical activity with relatively low muscle activation could contribute to glucose uptake.[21,22] In particular, although the mechanisms of the adverse influence of prolonged sitting time have not been precisely clarified, low activation of the large skeletal muscles involved in postural control could cause metabolic failure of lipid and glucose.[23] Given that pancreas cancer is regarded as related to insulin,[24,25] an increased risk of pancreas cancer with a long time spent sitting at work might be plausible.

Three metaanalyses, by Schmid et al,[3] Cong et al,[26] and Ma et al,[27] have all reported a positive association between occupational sitting time and colon cancer risk, with summary relative risks of 1.24 (95% CI = 1.09-1.41), 1.30 (95% CI = 1.20-1.40), and 1.24 (95% CI = 1.19-1.29), respectively. However, 1 cohort study[28] and 1 case-control study[29] in an Asian population included in these metaanalyses did not show a positive association. The lack of association in these previous studies[28,29] was reached by estimating the sitting time of participants based on job title. In the present study in Japanese men, our main results from self-reported occupational sitting time with relatively large sample sizes also showed no statistically significant association between occupational sitting time and colon cancer risk. However, we did observe a marginally positive linear trend (P for trend = 0.060)

between occupational sitting time and colon cancer risk in men when we undertook the same analysis using <1 h as reference (data not shown). Given that many studies in Europe and North America[3,26,27] have reported a positive association between occupational sitting time and colon cancer risk, and that obesity due to long sitting time could mediate increased risks for certain cancers, such as colorectal cancer, through shared mechanisms,[3] our results could suggest a slightly increased risk of colon cancer in men, as in previous studies.[3,26,27]

In women, occupational sitting time was significantly associated with lung cancer incidence in our study. To our knowledge, this is the first prospective cohort study to find a positive association between occupational sitting time and lung cancer risk. Our results are consistent with a cohort study that found that total sitting time, not occupational, was associated with increased risk of lung cancer in never-smokers[30] and a case-control study that reported an association between long sitting and an increased risk of lung cancer in Europe female workers.[31] In addition to the mechanism commonly proposed as a rationale for the association between sedentary behavior and cancer risk,[17,18] the positive association between occupational sitting time and lung cancer in women might imply the influence of other exposures, such as passive smoking, that have been reported to increase the risk of lung cancer at the workplace.[32] Weiderpass and colleagues have reported a significant association between sedentary work and increased risk of colon cancer in Finnish women,[16] whereas 2

TABLE 3 Hazard ratios for cancer incidence at total and specific sites according to daily occupational sitting time in women

	Occupational sitting time (h)					
	<1	1 to <3	3 to <5	5 to <7	≥7	P for trend[a]
	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)	HR (95% CI)	
Women						
Total						
Number of subjects	3305	3800	2435	1634	2103	
Person-years	38 209	43 884	27 731	18 630	24 587	
Number of cases	245	247	218	113	142	
Age- and area-adjusted HR	1.15 (0.96-1.37)	1.00 (ref)	1.40 (1.17-1.68)	1.12 (0.89-1.40)	1.10 (0.89-1.35)	.403
Multivariable HR	1.15 (0.97-1.38)	1.00 (ref)	1.38 (1.15-1.66)	1.09 (0.87-1.36)	1.08 (0.87-1.33)	.562
Esophagus						
Number of cases	3	2	3	0	0	
Age- and area-adjusted HR	1.89 (0.31-11.40)	1.00 (ref)	2.29 (0.38-13.79)	—	—	—
Multivariable HR	1.64 (0.25-10.75)	1.00 (ref)	2.38 (0.35-16.45)	—	—	—
Stomach						
Number of cases	28	36	23	20	20	
Age- and area-adjusted HR	0.90 (0.55-1.48)	1.00 (ref)	1.00 (0.59-1.68)	1.32 (0.76-2.29)	1.06 (0.61-1.83)	.569
Multivariable HR	0.89 (0.54-1.46)	1.00 (ref)	1.03 (0.61-1.74)	1.35 (0.78-2.36)	1.03 (0.59-1.81)	.696
Colorectal						
Number of cases	55	54	46	32	25	
Age- and area-adjusted HR	1.18 (0.81-1.72)	1.00 (ref)	1.35 (0.91-2.00)	1.47 (0.95-2.29)	0.94 (0.58-1.51)	.743
Multivariable HR	1.22 (0.84-1.78)	1.00 (ref)	1.26 (0.85-1.87)	1.36 (0.87-2.11)	0.94 (0.58-1.53)	.849
Colon						
Number of cases	40	41	36	23	19	
Age- and area-adjusted HR	1.15 (0.74-1.78)	1.00 (ref)	1.38 (0.88-2.16)	1.38 (0.83-2.31)	0.94 (0.54-1.62)	.886
Multivariable HR	1.20 (0.77-1.85)	1.00 (ref)	1.27 (0.81-2.00)	1.24 (0.74-2.09)	0.91 (0.52-1.60)	.967
Rectum						
Number of cases	15	13	10	9	6	
Age- and area-adjusted HR	1.28 (0.61-2.70)	1.00 (ref)	1.26 (0.55-2.87)	1.77 (0.75-4.15)	0.95 (0.36-2.50)	.681
Multivariable HR	1.27 (0.60-2.68)	1.00 (ref)	1.20 (0.52-2.76)	1.76 (0.74-4.16)	1.00 (0.37-2.69)	.821
Liver						
Number of cases	6	10	3	1	1	
Age- and area-adjusted HR	0.69 (0.25-1.90)	1.00 (ref)	0.50 (0.14-1.81)	0.27 (0.03-2.14)	0.23 (0.03-1.79)	.076
Multivariable HR	0.66 (0.24-1.84)	1.00 (ref)	0.58 (0.16-2.13)	0.31 (0.04-2.49)	0.30 (0.04-2.20)	.109
Pancreas						
Number of cases	10	8	10	7	4	
Age- and area-adjusted HR	1.43 (0.56-3.63)	1.00 (ref)	2.05 (0.81-5.21)	2.27 (0.82-6.27)	1.01 (0.30-3.39)	.582
Multivariable HR	1.36 (0.53-3.46)	1.00 (ref)	2.10 (0.82-5.37)	2.12 (0.75-5.96)	0.90 (0.26-3.07)	.858
Lung						
Number of cases	25	13	20	6	17	
Age- and area-adjusted HR	2.23 (1.14-4.37)	1.00 (ref)	2.50 (1.24-5.02)	1.19 (0.45-3.14)	2.72 (1.31-5.64)	.028
Multivariable HR	2.17 (1.11-4.26)	1.00 (ref)	2.63 (1.30-5.30)	1.26 (0.48-3.35)	2.80 (1.33-5.90)	.013
Kidney						
Number of cases	3	2	4	3	0	
Age- and area-adjusted HR	1.82 (0.30-10.94)	1.00 (ref)	3.25 (0.59-17.83)	4.46 (0.73-27.07)	—	—

(Continues)

TABLE 3 (Continued)

	Occupational sitting time (h)					
	<1	1 to <3	3 to <5	5 to <7	≥7	P for trend[a]
	HR (95% CI)	HR	HR (95% CI)	HR (95% CI)	HR (95% CI)	
Multivariable HR	1.73 (0.29-10.44)	1.00 (ref)	3.40 (0.61-18.91)	4.15 (0.66-26.11)	—	—
Bladder						
Number of cases	3	5	2	3	2	
Age- and area-adjusted HR	0.79 (0.19-3.33)	1.00 (ref)	0.61 (0.12-3.15)	1.60 (0.38-6.80)	0.86 (0.16-4.53)	.927
Multivariable HR	0.83 (0.20-3.50)	1.00 (ref)	0.54 (0.10-2.81)	1.42 (0.33-6.13)	0.79 (0.14-4.27)	.927
Breast						
Number of cases	44	43	38	20	29	
Age- and area-adjusted HR	1.18 (0.77-1.80)	1.00 (ref)	1.40 (0.91-2.17)	1.08 (0.63-1.83)	1.18 (0.73-1.89)	.572
Multivariable HR[b]	1.21 (0.79-1.84)	1.00 (ref)	1.39 (0.89-2.15)	1.04 (0.61-1.78)	1.11 (0.69-1.81)	.618
Ovarian						
Number of cases	7	7	4	0	6	
Age- and area-adjusted HR	1.13 (0.40-3.24)	1.00 (ref)	0.86 (0.25-2.95)	—	1.45 (0.48-4.35)	—
Multivariable HR[b]	1.11 (0.38-3.11)	1.00 (ref)	0.93 (0.27-3.22)	—	1.51 (0.48-4.72)	—
Endometrial						
Number of cases	17	13	8	8	4	
Age- and area-adjusted HR	1.45 (0.70-2.99)	1.00 (ref)	1.01 (0.42-2.43)	1.49 (0.62-3.60)	0.51 (0.17-1.59)	.463
Multivariable HR[b]	1.37 (0.66-2.83)	1.00 (ref)	0.99 (0.41-2.40)	1.41 (0.58-3.47)	0.49 (0.15-1.52)	.314
Other						
Number of cases	48	58	58	17	36	
Age- and area-adjusted HR	0.96 (0.66-1.41)	1.00 (ref)	1.58 (1.10-2.27)	0.71 (0.41-1.22)	1.21 (0.80-1.84)	.903
Multivariable HR	0.97 (0.66-1.42)	1.00 (ref)	1.53 (1.06-2.21)	0.68 (0.39-1.18)	1.16 (0.75-1.78)	.885

Note: Multivariable hazard ratio (HR) adjusted for age (continuous), area (10 public health center areas), history of diabetes (no, yes), smoking status (never, former or current), alcohol intake status (nondrinkers or occasional drinkers, 1 to <150 g/wk, or ≥150 g/wk), body mass index (<18.5, 18.5-24.9, 25-29, or ≥30), coffee (almost none, 1-4 times/wk, 1-2 cups/d, or ≥3 cups/d), walking time at work (continuous), strenuous time at work (continuous), moderate-to-vigorous physical activity time in leisure time (continuous), type of job (primary industry, or secondary or tertiary industry), and total working hours (continuous).

Abbreviations: —, not applicable; CI, confidence interval; ref, reference.

[a]P for trend was tested by assignment of ordinal values into 4 groups (1 to <3 h, 3 to <5 h, 5 to <7 h, and ≥7 h/d).

[b]Additional adjusted for age at menopause (<44, 45-49, ≥50 y, or unknown).

cohort studies identified null associations between occupational sitting time and colon[28] and colorectal[33] cancer risk in women. With regard to breast cancer, the World Cancer Research Fund reports state that physical activity probably decreases risk of breast cancer (postmenopausal),[34,35] even though no significant association between occupational sitting time and breast cancer risk was reported in 2 cohort[8,36] or 4 case-control studies.[32,37-39] The reason for the discrepancy in previous results by difference in exposure to physical activity and occupational sitting time is assumed to be that sedentary leisure-time activities, such as sitting time to watch television, tend to be associated with adverse health outcomes because of the unhealthy behaviors that accompany them.[40] Given that our study had a high proportion of women who were unemployed or working in home duties that we excluded for analysis, further research is required regarding

the association between recreational sitting time and cancer, although our results support previous findings of a null association between occupational sitting time and cancer incidence in women.

We also found a statistically significant association between occupational sitting time and pancreas cancer risk in men with a low BMI, but not in men with a high BMI, although the interaction between occupational sitting time and BMI was not statistically significant. Body fatness is a risk factor for pancreas cancer incidence.[34,35] A decrease in time spent sitting at work might be more preventive against pancreas cancer in men with a low BMI, who are less affected by body fatness, than in men who are overweight or obese.

We found an increased risk of pancreas cancer with 3 h or more occupational sitting time in men with both short and long MVPA time at leisure time, although this was not statistically significant.

TABLE 4 Hazard ratios for total and pancreas cancer incidence by body mass index and moderate-to-vigorous physical activity in leisure time in men

| | Occupational sitting time (h) | | |
| | <3 | ≥3 | |
	HR	HR (95% CI)	P for interaction
Total			
BMI at baseline <25			
Number of cases	1091	890	
Multivariable HR[a]	1.00	1.08 (0.99-1.19)	.831
BMI at baseline ≥25			
Number of cases	425	436	
Multivariable HR[a]	1.00	1.03 (0.89-1.18)	
Short MVPA time (<30 min/wk) in leisure time at baseline			
Number of cases	851	618	
Multivariable HR[b]	1.00	1.08 (0.97-1.21)	.315
Long MVPA time (≥30 min/wk) in leisure time at baseline			
Number of cases	665	708	
Multivariable HR[b]	1.00	1.05 (0.94-1.18)	
Pancreas			
BMI at baseline < 25			
Number of cases	26	36	
Multivariable HR[a]	1.00	1.83 (1.07-3.13)	.684
BMI at baseline ≥ 25			
Number of cases	10	14	
Multivariable HR[a]	1.00	1.53 (0.65-3.61)	
Short MVPA time (<30 min/wk) in leisure time at baseline			
Number of cases	22	27	
Multivariable HR[b]	1.00	1.74 (0.96-3.15)	.965
Long MVPA time (≥30 min/wk) in leisure time at baseline			
Number of cases	14	23	
Multivariable HR[b]	1.00	1.80 (0.89-3.66)	

Abbreviations: CI, confidence interval; HR, hazard ratio; MVPA, moderate-to-vigorous physical activity.

[a]Adjusted for age (continuous), area (10 public health center areas), history of diabetes (no, yes), smoking status (never, former or current), alcohol intake status (non - or occasional drinkers, 1 to <150 g/wk, or ≥150 g/wk), coffee (almost none, 1-4 times/wk, 1-2 cups/d, or ≥3 cups/d), walking time at work (continuous), strenuous time at work (continuous), moderate-to-vigorous physical activity time in leisure time (continuous), type of job (primary industry, or secondary or tertiary industry), and total working hours (continuous).

[b]Adjusted for age (continuous), area (10 public health center areas), history of diabetes (no, yes), smoking status (never, former or current), alcohol intake status (nondrinkers or occasional drinkers, 1 to <150 g/wk, or ≥150 g/wk), body mass index (BMI; <18.5, 18.5-24.9, 25-29, or ≥30), coffee (almost none, 1-4 times/wk, 1-2 cups/d, or ≥3 cups/d), walking time at work (continuous), strenuous time at work (continuous), type of job (primary industry, or secondary or tertiary industry), and total working hours (continuous).

These results might suggest that reducing occupational sitting time could lead to a decreased risk of pancreas cancer in men, regardless of leisure-time physical activity.

Although we speculated that participants with an extremely short occupational sitting time would experience adverse effects because they spent a longer time standing at work than those with a long occupational sitting time (occupational sitting time <1 h vs >7 h; mean standing time 5.6 hours vs 3.0 hours), there were no associations between extremely short occupational sitting time and cancer incidence in this study except for lung cancer in women. Smith et al reported that occupations that predominantly involve standing were associated with an increased risk of heart disease.[41] The reason for the increased risk of lung cancer in women in this study is not clear because the mechanisms of the adverse effect of incident heart disease with prolonged standing time at work, such as blood pooling in the lower limbs and increased hydrostatic venous pressure, and those of cancer development are different.

Strengths of this study include its prospective design, large sample size, high survey response rate (83.2%), and low rate of loss of follow-up (0.1%). Because information on occupational sitting time was obtained before a subsequent cancer diagnosis, recall bias was unlikely to have influenced the results. Furthermore, the cancer registry in this study possesses sufficient quality to reduce the likelihood of misclassification of outcomes.

Several limitations of our study also warrant mention. First, because occupational sitting time was determined using a self-reported questionnaire and included sitting time for commuting, we cannot rule out the possibility that our results were affected by misclassification of exposure. Nevertheless, we feel this approach is comparable to or an improvement over several previous cohort studies, which also estimated occupational sitting time by questionnaire, or by estimating from the individual participant's job title. Moreover, any misclassification of exposure would likely influence the results towards null. Second, we could not evaluate the content of the sitting time, such as with regard to interruptions in sitting time. Third, despite the large sample size and long follow-up period, incidence of some cancers was small in women who had an occupational sitting time of over 5 hours. Thus, it was not possible to evaluate the association between occupational sitting time and some cancer risks. Fourth, we obtained information on education from participants in Cohort I only. We therefore adjusted for education level using Cohort I subjects only, but found no substantial difference in the results. Finally, other unknown risk factors might have confounded the association between occupational sitting time and cancer. Although we adjusted for and stratified by potential confounding variables, we could not fully exclude the effects of unmeasured confounders.

In conclusion, our study found a positive association between long occupational sitting time and increased risk of pancreas cancer in men and lung cancer in women. Given that adults spend most of their working hours sitting, our findings suggest that reducing long times spent sitting at work could be important for cancer prevention.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.