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Original Investigation

Smoking and Long-Term Sick Leave in a Japanese Working Population: Findings of the Japan Epidemiology Collaboration on Occupational Health Study

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Abstract

Background: Few studies have investigated the association between tobacco smoking and sick leave (SL) in Japan.

Methods: We followed 70 896 workers aged 20–59 years (60 133 males, 10 763 females) between April 2012 and March 2017. A Cox proportional hazards model was used to investigate the associations between smoking (smoking status and intensity) and long-term SL (ie, SL lasting ≥30 consecutive days). Cause-specific analyses were also conducted.

Results: A total of 1777 people took long-term SL during a follow-up of 307 749 person years. Compared with never-smokers, current smokers were at a higher risk of long-term SL (hazard ratio [HR] = 1.32; 95% confidence interval [CI] = 1.19 to 1.48). Cause-specific analyses revealed that current smoking was associated with a higher risk of SL due to all physical disorders (HR = 1.44, 95% CI = 1.22 to 1.69), cancer (HR = 1.49, 95% CI = 1.10 to 2.01), cardiovascular disease (CVD; HR = 2.16, 95% CI = 1.31 to 3.55), and injuries/external causes (HR = 1.83, 95% CI = 1.31 to 2.58). Former smokers were at a higher risk of SL due to cancer at a borderline significance level (HR = 1.38, 95% CI = 0.99 to 1.92). Low-intensity smoking (ie, 1–10 cigarettes smoked per day) was associated with all-cause SL, SL due to CVD, and SL due to injuries/external causes compared with never-smokers. Conclusion: In a large cohort of working-age Japanese, smoking was associated with a greater risk of long-term SL. Greater effort is needed to mitigate disease burden associated with smoking at workplace in Japan.

Implications: Our study contributes to the literature on the association between smoking and SL in several ways. First, the study was conducted among a Japanese working population. While the association has been extensively studied in Western setting, few attempts have been made elsewhere. Second, cause-specific analyses were undertaken in our study. Third, we paid attention to the effect of low-intensity smoking on SL given that there is growing evidence of an elevated health risk associated with low-intensity smoking.

Introduction

Tobacco smoking continues to be a leading risk factor for premature mortality and disability. Smoking killed an estimated 6.4 million people in 2015, or 11.5% of all deaths worldwide, and it caused a global loss of nearly 150 million disability-adjusted life years. While a growing number of countries have reached the highest level of achievement for at least one of the progress indicators for the World Health Organization Framework Convention on Tobacco Control (WHO FCTC), more effort is needed to mitigate the disease burden associated with tobacco smoking.

Sick leave (SL) is a negative health outcome that has been studied in relation to smoking. A meta-analysis of 29 longitudinal studies involving 70 000 workers showed that current and former smokers were at 33% and 14% higher risks of SL, respectively, compared with those who had never smoked.³ More recently, Virtanen et al.⁴ used individual-level information on SL lasting for nine consecutive days or longer collected in four cohorts from the United Kingdom, France, and Finland and showed that smoking was associated with SL due to circulatory diseases, respiratory diseases, depressive disorders, and external causes. As SL has imposed large costs on society both directly (eg, medical expenditures) and indirectly (eg, decreased work productivity and increased social insurance claims), ^{5,6} quantifying the negative effects of smoking on SL is of public health significance.

Nevertheless, several issues remain to be addressed. First, few studies have investigated the cause-specific association between to-bacco smoking and SL.^{4,7,8} Second, there have been few extensive analyses of the association between smoking intensity and SL. This may be an important omission, as there is growing evidence of an elevated health risk associated with low-intensity smoking.^{9,10} Third, while the association has been studied extensively in Western settings,^{3,4} few attempts have been made elsewhere, including Japan, which has fallen far behind other high-income countries in terms of most of the WHO FCTC progress indicators.^{11,12} To address

these gaps, we conducted a cause-specific analysis of the association between smoking and medically certified long-term SL using information collected in the Japan Epidemiology Collaboration on Occupational Health (J-ECOH) study.

Methods

J-ECOH Study

The J-ECOH study is an ongoing multicenter epidemiological study of workers from 12 companies in various industries. We collected information via annual health examinations that employers are obliged to provide to their employees under the Industrial Safety and Health Act. A study-specific SL registry was established in April 2012 to collect information on long-term SL (ie, SL that lasts ≥30 consecutive days). The details of the J-ECOH Study have been described previously.^{13,14}

Participants

Of the 97 226 individuals from the 12 participating companies who underwent health checkups in fiscal 2011 (ie, the period between April 1, 2011 and March 31, 2012), we excluded those who worked for two companies that did not provide information on former smoking (n = 4814; Figure 1). We also excluded (1) those who were aged less than 20 years or 60 or more years in 2011 given that the minimum smoking age is 20 years in Japan and that people tend to retire instead of taking long-term SL when they are aged 60 or more years (n = 8029), (2) those with missing data on smoking status (n = 6216), (3) those who reported a history of cancer, cardiovascular disease (CVD), or psychiatric disorders (n = 3255) to avoid reverse causation (ie, those with these disorders stopped smoking following the diagnoses), and (4) those who did not attend any subsequent health checkups, for whom we had no information on mortality or long-term SL since April 2012 (n = 4016). Ultimately, the analyses included 70 896 individuals: 60 133 men and 10 763 women.

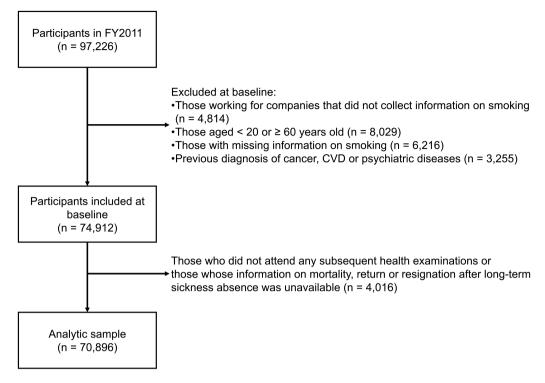


Figure 1. Participants in the Japan Epidemiology Collaboration on Occupational Health Study (2012–2017).

Smoking Status

We used self-reported information to define smoking status (ie, never, former, or current smokers). To determine whether there is a dose–response relationship between the number of cigarettes smoked and the incidence of SL, we also categorized the current smokers into three groups based on the number of cigarettes per day: that is, 1–10, 11–20, and 21 or more cigarettes. Information on the number of cigarettes per day was available only for six companies.

Definition of Outcome

Information on the causes of SL was obtained from the medical certificates written by attending physicians (not by occupational physicians); the employees submit these medical certificates to apply for paid SL. We used the International Classification of Diseases 10th revision (ICD-10) to classify the diagnoses; more specifically, we retrieved an appropriate ICD-10 code from the Japanese standard disease-code master and when we had unmatched certificates, multiple occupational physicians of the J-ECOH study group independently coded the certificate and checked if there were discrepancies. All conflicts were resolved through discussion among the members.

The study outcome is the incidence of SL that lasted 30 consecutive days or longer between April 2012 and March 2017. We further classified SL into SL due to (1) mental disorders (ICD-10: F00–F99), (2) injuries/external causes (injury, poisoning, and other consequences of external causes: S00–T98), and (3) physical disorders (SL other than specified above). For physical disorders, we further investigated whether smoking status was linked with SL due to cancer (C00–D48), CVD (I00–I99), and musculoskeletal disease (M00–M99), which were reported to be three major physical disorders that caused long-term SL in this population. ¹⁴ We focused on the incidence of the first SL episode; those who took long-term SL multiple times were censored on the date of the first

episode and were not included in the analysis even if the subsequent SL was caused by other disorders.

Covariates

Information on the following covariates was collected at baseline (ie, FY 2011). Body height and weight were measured to compute body mass index (BMI; kg/m²). Blood pressure was measured in a sitting position by an automated sphygmomanometer. Hypertension was defined as systolic blood pressure ≥140 mm Hg, diastolic blood pressure ≥90 mm Hg, or the use of antihypertensive medication. Diabetes was defined as a fasting plasma glucose ≥126 mg/dL (7.0 mmol/L), HbA1c ≥6.5% (48 mmol/mol), or the current use of antidiabetic medication. Plasma glucose was measured using an enzymatic method or the glucose oxidase peroxidative electrode method and HbA1c was measured using a latex agglutination immunoassay, high-performance liquid chromatography, or an enzymatic method. Dyslipidemia was defined as triglyceride ≥150 mg/dL, low-density lipoprotein-cholesterol ≥140 mg/dL, or high-density lipoproteincholesterol <40 mg/dL measured with enzymatic methods or under treatment for dyslipidemia.

Statistical Analyses

The descriptive characteristics of the study participants were compared by smoking status using analysis of variance for continuous variables and Pearson's chi-square test for categorical variables. Person time was calculated from March 31, 2012 (ie, one day before the starting date of data collection) to the first day of long-term SL or the date of the last participation in a health examination, whichever occurred first. Those who died during the study period were censored on the dates that they died.

A Cox proportional hazards model was used to investigate the association between the baseline smoking status (ie, never, former, or current smoker) and the incidence of long-term SL. Model 1 adjusted

for age (years, continuous) and sex (men and women), while accounting for the hierarchical structure of the dataset (ie, employees nested in each work-site). Model 2 further adjusted for baseline BMI categories (<18.5; 18.5–24.9; 25.0–29.9; and ≥30 kg/m²), hypertension, diabetes, and dyslipidemia. Cause-specific analyses were then performed; that is, SL due to mental disorders, physical disorders, or injuries/external causes. Among physical disorders, cancer, CVD, and musculoskeletal disorders were investigated separately in relation to smoking status.

To see if a dose–response relationship existed between tobacco consumption and SL, we ran additional analyses with a different exposure definition (ie, never-smoker, those who smoked 1–10 cigarettes/day, those who smoked 11–20 cigarettes/day, or those who smoked 21 or more cigarettes/day). Cause-specific analyses were also performed with this exposure definition.

All statistical tests were two sided. The results are shown in terms of hazard ratios (HRs) and their corresponding 95% confidence intervals (CIs). We also calculated *p*-values for linear trends in the analyses of smoking intensity. The analyses were performed using Stata ver. 15.0 (Stata Corp, College Station, TX).

Results

Table 1 shows the basic characteristics of the study participants. At baseline, current, former, and never-smokers comprised 33.9%, 19.7%, and 46.5% of the cohort, respectively. Former smokers were older and more likely to have hypertension and dyslipidemia compared with never-smokers and current smokers.

During a follow-up of 307 749 person years (median follow-up 5 years), 1777 participants took long-term SL (ie, 2.5% of the study participants). Of the SL episodes, 40.1% were due to mental disorders (F00–F99), 10.5% for injuries/external causes (S00–T98), and the remaining 49.5% were attributable to physical disorders, which included cancer (C00–D48; 15.4%), musculoskeletal disease (M00–M99; 9.1%), and CVD (I00–I99; 5.0%).

Table 2 shows the results of a Cox hazards regression analysis investigating the association between baseline smoking status and

long-term SL. Compared with never-smokers, current smokers had a significantly higher risk of all-cause long-term SL (HR = 1.32, 95% CI = 1.19 to 1.48); this association remained significant after adjusting for baseline hypertension, diabetes, and dyslipidemia. We did not find evidence of a significant association among former smokers. When cause-specific analyses were undertaken, current smokers were at higher risk of long-term SL due to physical disorders (HR = 1.44, 95% CI = 1.22 to 1.69), cancer (HR = 1.49, 95% CI = 1.10 to 2.01), CVD (HR = 2.16, 95% CI = 1.31 to 3.55), and injuries/external causes (HR = 1.83, 95% CI = 1.31 to 2.58). These associations remained significant in the fully adjusted models. Former smokers were at higher risk of long-term SL due to cancer only at a marginally significant level (HR = 1.38, 95% CI = 0.99 to 1.92).

Our analysis of the association in relation to smoking intensity Table 3 revealed that compared with those who had never smoked, those who smoked 1–10, 11–20, and 21+ cigarettes/day were at 1.30 (95% CI = 1.10 to 1.53), 1.29 (95% CI = 1.14 to 1.47), and 1.45 (95% CI = 1.17 to 1.80) times higher risk of all-cause long-term SL, respectively (*p* for trend <.001). Cause-specific analyses showed that there was a dose–response relationship for SL due to physical disorders (those who smoked 11–20 cigarettes/day: HR = 1.45 [95% CI = 1.20 to 1.74]; those who smoked 21+ cigarettes/day: HR = 1.52 [95% CI = 1.13 to 2.05; *p* for trend <.001]). When considering SL due to CVD and injuries/external causes, we found that the risk of long-term SL associated with smoking was elevated, even in the lowest intensity group (SL due to CVD: HR = 2.50 [95% CI = 1.19 to 5.27]; SL due to injuries/external causes: HR = 2.04 [95% CI = 1.24 to 3.33]).

Discussion

In this large-scale prospective cohort study of working-age Japanese, current smoking was associated with a significantly higher risk of long-term SL due to all causes (HR = 1.32), all physical disorders (HR = 1.44), and injuries/external causes (HR = 1.83). Of the physical disorders, cancer and CVD had higher risks of long-term SL among current smokers (cancer, HR = 1.49; CVD, HR = 2.16).

Table 1. Basic characteristics of the study participants in the Japan Epidemiology Collaboration on Occupational Health Study shown by baseline smoking status (2011)

	Whole participants	Smoking status			
		Never-smoker	Former smoker	Current smoker	
Number of subjects	70 896	32 947	13 939	24 010	
Age, mean [SD]	41.6 [10.4]	40.1 [10.5]	45.2 [9.1]	41.5 [10.3]	
Male, n (%)	60 133 (84.8)	23 999 (72.8)	13 308 (95.5)	22 826 (95.1)	
Body mass index categories, n (%)					
<18.5	3728 (5.3)	2291 (7.0)	335 (2.4)	1102 (4.6)	
18.5-24.9	48 380 (68.2)	23 148 (70.3)	9358 (67.1)	15 874 (66.1)	
25.0-29.9	15 578 (22.0)	6164 (18.7)	3682 (26.4)	5732 (23.9)	
30+	3210 (4.5)	1344 (4.1)	564 (4.0)	1302 (5.4)	
Hypertension, n (%)	11 980 (16.9)	4769 (14.5)	3227 (23.2)	3984 (16.6)	
Diabetes, n (%)	9647 (13.6)	4563 (13.8)	1557 (11.2)	3527 (14.7)	
Dyslipidemia, n (%)	28 333 (40.0)	10 714 (32.5)	6580 (47.2)	11 039 (46.0)	
Smoking intensity, n (%) [†]					
1–10				5958 (25.7)	
11–20				14 116 (60.9)	
20+				3095 (13.4)	

Table 2. Adjusted hazard ratios (95% confidence intervals) for long-term sick leave among the participants in the Japan Epidemiology Collaboration on Occupational Health Study (2012–2017) shown by baseline smoking status

	Never-smoker	Former smoker	Current smoker
Number of subjects	32 947	13 939	24 010
Person years	142 576	60 546	104 627
1. All-cause sick leave			
No. of events	777	294	706
Model 1	1.00 (ref.)	0.93 (0.80, 1.07)	1.32 (1.19, 1.48)
Model 2	1.00 (ref.)	0.92 (0.79, 1.06)	1.31 (1.17, 1.46)
2. Sick leave due to mental disord	ders		
No. of events	333	101	278
Model 1	1.00 (ref.)	0.83 (0.66, 1.04)	1.13 (0.95, 1.33)
Model 2	1.00 (ref.)	0.82 (0.65, 1.03)	1.10 (0.93, 1.30)
3. Sick leave due to all physical d	lisorders		
No. of events	371	165	342
Model 1	1.00 (ref.)	1.04 (0.85, 1.26)	1.44 (1.22, 1.69)
Model 2	1.00 (ref.)	1.02 (0.84, 1.24)	1.42 (1.21, 1.67)
3a. Sick leave due to cancer			
No. of events	109	66	98
Model 1	1.00 (ref.)	1.38 (0.99, 1.92)	1.49 (1.10, 2.01)
Model 2	1.00 (ref.)	1.37 (0.98, 1.91)	1.49 (1.10, 2.00)
3b. Sick leave due to cardiovascu	ılar disease		
No. of events	24	13	52
Model 1	1.00 (ref.)	0.70 (0.35, 1.39)	2.16 (1.31, 3.55)
Model 2	1.00 (ref.)	0.67 (0.34, 1.34)	2.09 (1.26, 3.45)
3c. Sick leave due to musculoske	letal disorders		
No. of events	74	28	59
Model 1	1.00 (ref.)	0.84 (0.53, 1.34)	1.19 (0.83, 1.73)
Model 2	1.00 (ref.)	0.84 (0.53, 1.33)	1.19 (0.82, 1.73)
4. Sick leave due to injuries/exter	rnal causes		
No. of events	72	28	86
Model 1	1.00 (ref.)	0.95 (0.60, 1.50)	1.83 (1.31, 2.58)
Model 2	1.00 (ref.)	0.94 (0.59, 1.49)	1.84 (1.31, 2.59)

Model 1 adjusted for age, sex; model 2 further adjusted for baseline and body mass index categories (<18.5; 18.5–24.9; 25.0–29.9; 30+ kg/m²), hypertension, diabetes, and dyslipidemia. The analysis was stratified by work sites. One participant did not provide information on the cause of sick leave. ref = reference category.

Former smokers were at higher risk of SL due to cancer at a marginally significant level (HR = 1.38). In analyzing the association between the intensity of smoking and SL, dose–response relationships were observed for all-cause SL and SL due to physical disorders. Note that the risks of long-term SL due to CVD and injuries/external causes were even elevated among those in the lowest intensity category (ie, those who smoked 1–10 cigarettes/day).

Our findings of an elevated risk of long-term SL among current smokers accord with the literature. For example, Quist et al. ¹⁵ showed that current smokers were at a higher risk of long-term SL among female health care workers in Denmark. In a study of Swedish women from the public sector, Vingard et al. ¹⁶ showed that daily smoking was associated with long-term SL. Christensen et al. ¹⁷ showed that, in Denmark, heavy smoking, but not moderate smoking, was linked to long-term sickness in both sexes. Our study extends these studies by reporting the smoking-related adverse effects on the incidence of SL in a non-Western setting.

Our cause-specific analyses revealed that current smoking was linked with SL due to physical disorders and suggests that SL due to cancer and CVD contributed to this association. While we are not aware of any studies that specifically investigated the association between smoking and physical disorders as a group, our findings are in line with the broader literature, which reported the adverse effects of tobacco smoking on all-cause mortality, CVD, and cancer. Virtanen et al. A also reported an association between smoking and SL due to

circulatory disease, although their definition of SL differed (ie, SL lasting more than 9 days).

In our study, current smoking was also associated with the risk of SL due to injuries/external causes. Several studies have shown that accidents/injuries are more likely to occur among smokers at the workplace^{19–22} or in general.²³ One possible mechanism is nicotine withdrawal symptoms, which include irritation, restlessness, and increased difficulty concentrating experienced a few hours after nicotine abstinence; these symptoms in smokers might underlie the increased risk of long-term SL due to accidents/injuries. The observed association might be partly explained by confounders that affect both cigarette smoking and injuries/accidents (eg, low socioeconomic status^{24,25} and neuropsychiatric conditions that are associated with risk-taking behavior^{26–28}).

We did not find evidence of a significant association between former smoking and all-cause SL, while the risk of SL due to cancer was elevated among former smokers. Studies have reported a significant association between former smoking and all-cause SL; for example, Ferrie et al.²⁹ showed that former smokers were at an elevated risk of short- and long-term leave in men (rate ratios = 1.10 [95% CI = 1.04 to 1.17] and 1.16 [95% CI = 1.06 to 1.27], respectively). Christensen et al.¹⁷ reported an elevated risk of SL among female former smokers, while they did not find evidence of a significant association among male former smokers. While more studies are needed, our null-finding might have resulted from a difference in the

Table 3. Adjusted hazard ratio (95% confidence intervals) for long-term sick leave among the participants in the Japan Epidemiology Collaboration on Occupational Health Study (2012–2017) shown by baseline smoking intensity

		Current smoker			
	Never-smoker	1–10	11–20	≥21	$p_{\rm trend}$
Number of subjects	32 947	5958	14 116	3095	
Person years	142 576	25 871	61 636	13 416	
1. All-cause sick leave					
No of events	777	174	412	108	
Model 1	1.00 (ref.)	1.30 (1.10, 1.53)	1.29 (1.14, 1.47)	1.45 (1.17, 1.80)	<.001
Model 2	1.00 (ref.)	1.29 (1.09, 1.53)	1.27 (1.12, 1.45)	1.38 (1.12, 1.72)	<.001
2. Sick leave due to ment	al disorders				
No of events	333	84	157	35	
Model 1	1.00 (ref.)	1.21 (0.95, 1.54)	1.06 (0.87, 1.30)	1.31 (0.90, 1.89)	.17
Model 2	1.00 (ref.)	1.20 (0.94, 1.53)	1.04 (0.85, 1.27)	1.24 (0.86, 1.79)	.30
3. Sick leave due to all pl	nysical disorders				
No of events	371	68	207	59	
Model 1	1.00 (ref.)	1.23 (0.94, 1.59)	1.45 (1.20, 1.74)	1.52 (1.13, 2.05)	<.001
Model 2	1.00 (ref.)	1.22 (0.94, 1.59)	1.43 (1.18, 1.72)	1.45 (1.08, 1.96)	<.001
3a. Sick leave due to cano	cer				
No of events	109	20	62	16	
Model 1	1.00 (ref.)	1.39 (0.86, 2.26)	1.61 (1.14, 2.28)	1.37 (0.78, 2.42)	.008
Model 2	1.00 (ref.)	1.39 (0.85, 2.26)	1.60 (1.13, 2.27)	1.35 (0.76, 2.39)	.01
3b. Sick leave due to card	liovascular disease				
No. of events	24	10	30	11	
Model 1	1.00 (ref.)	2.50 (1.19, 5.27)	2.00 (1.14, 3.48)	2.10 (0.98, 4.50)	.004
Model 2	1.00 (ref.)	2.47 (1.17, 5.20)	1.91 (1.09, 3.34)	1.97 (0.92, 4.20)	.008
3c. Sick leave due to mus	culoskeletal disorders				
No. of events	74	11	39	7	
Model 1	1.00 (ref.)	0.95 (0.50, 1.81)	1.30 (0.85, 1.99)	1.05 (0.46, 2.37)	.38
Model 2	1.00 (ref.)	0.95 (0.50, 1.80)	1.29 (0.84, 1.97)	1.01 (0.44, 2.28)	.42
4. Sick leave due to injuri	ies/external causes				
No. of events	72	22	48	14	
Model 1	1.00 (ref.)	2.04 (1.24, 3.33)	1.80 (1.21, 2.70)	1.89 (1.01, 3.53)	<.001
Model 2	1.00 (ref.)	2.03 (1.24, 3.33)	1.80 (1.20, 2.69)	1.89 (1.01, 3.54)	<.001

Model 1 adjusted for age and sex; model 2 further adjusted for baseline and body mass index categories (<18.5; 18.5–24.9; 25.0–29.9; 30+ kg/m²), hypertension, diabetes, and dyslipidemia. The analysis was stratified by work sites.

composition of the causes of SL from the previous studies, given that harmful effects of smoking after cessation may persist differently by health outcomes (eg, a longer effect on cancer than on CVD).^{30,31} Notwithstanding the above, our study provides supporting evidence that the harmful effect of smoking on cancer persists after quitting smoking when we used SL as the study outcome.

Low-intensity smoking was also shown to be associated with all-cause SL and SL due to CVD and injuries/external causes in this study. There is accumulating evidence suggesting the negative health effects of low-intensity smoking. For example, Inoue-Choi et al. 9,10 have linked low-intensity smoking to all-cause mortality and mortality due to cancer, CVD, and respiratory diseases using information collected from a middle-aged to elderly population (aged 59–82 years at baseline) in the United States. In their meta-analysis of 141 cohort studies, Hackshaw et al. 32 found that no safe level of smoking existed for CVD. While we did not find evidence of an elevated risk among the lowest intensity group in relation to SL due to cancer, the public should be made aware of the elevated risk of SL associated with low-intensity smoking.

We did not find any evidence of a significant association between smoking and SL due to mental disorders, which contributed the most to long-term SL in our study. Previous findings regarding the association between smoking and mental disorders are conflicting. A recent meta-analysis showed that baseline smoking

was associated with an increased risk of depression, ^{33,34} although a causal relationship between smoking and mental disorders (ie, depression and anxiety) was not supported in a Mendelian randomization analysis. ³⁵ Furthermore, we did not find a significant association between smoking and SL due to musculoskeletal disease, while previous studies have linked smoking to SL due to unspecific back or neck pain. ^{7,8} One possible explanation for this discrepancy may be the different definitions of the duration of SL. For example, Tsai et al. ⁸ reported that three quarters of those who took SL because of musculoskeletal disorders returned to work within 2 weeks, which was not captured with the definition used in our study.

Several limitations should be borne in mind when interpreting our findings. First, we did not collect information on SL that lasted more than 30 days. While our aim was to investigate the effect of smoking on severer forms of SL, results may have been different when we had included SL that lasted for a shorter period of time. Second, measurement errors might have biased the study findings; for example, information on smoking status was self-reported, which might have been influenced by social desirability bias. It was also assessed only at baseline and we did not collect information on the cumulative effect of past smoking. Some participants might have reduced the number of cigarettes due to their current health conditions; this can lead to underestimation of the effect among

current smokers and overestimation of the effect among former smokers. In addition, we used information on hypertension, diabetes, and dyslipidemia, which were collected only once at baseline. Third, our study participants were mostly men working in large companies. Our results might have differed if we had had information from those working in small companies, those who were self-employed, or more females. Fourth, we lacked information on exposure to secondhand smoke, which suggests that the association between smoking and SL might have been underestimated. Fifth, we had no information on alcohol consumption, which is a possible confounder in the association between smoking and SL. Lastly, given that some cause-specific analyses might have been underpowered, more studies are needed to draw conclusions, particularly those on pregnancy-related disorders or types of cancer specific to females.

Despite the limitations described above, this study has several strengths. Most importantly, we examined the health effects of smoking on SL, which is one of the indicators that can best capture disease burden in the working-age population. Identifying the adverse health effects of smoking in this population may inform better effort to mitigate disease burden associated with smoking. Second, this study was conducted in Japan, where there is room for improvement as regards the WHO FCTC progress indicators. ^{11,12} Third, we conducted cause-specific analyses as well as the analyses focusing on the effects of low-intensity smoking, both of which facilitate our understanding of the health effects of smoking.

Conclusions

Our study of a Japanese working population showed that current smoking was associated with higher risks of all-cause SL and SL due to physical disorders, cancers, and CVDs and SL due to injuries/external causes. An elevated risk among former smokers was observed in the cause-specific analyses of SL due to cancer.

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Declaration of Interests

None declared.

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References

- Global Burden of Disease Tobacco Collaborators. Smoking prevalence and attributable disease burden in 195 countries and territories, 1990– 2015: a systematic analysis from the Global Burden of Disease Study 2015. *Lancet*. 2017;389(10082):1885–1906.
- World Health Organization. WHO Report on the Global Tobacco Epidemic, 2017: Monitoring Tobacco Use and Prevention Policies: Executive Summary. Geneva: 2017.

- Weng SF, Ali S, Leonardi-Bee J. Smoking and absence from work: systematic review and meta-analysis of occupational studies. Addiction. 2013;108(2):307–319.
- Virtanen M, Ervasti J, Head J, et al. Lifestyle factors and risk of sickness absence from work: a multicohort study. Lancet Public Health. 2018;3(11):e545-e554.
- Hensing G, Wahlstrom R. Chapter 7. Sickness absence and psychiatric disorders. Scand J Public Health Suppl. 2004;32:152–180.
- World Health Organization. Protecting workers' health. 2017; https:// www.who.int/news-room/fact-sheets/detail/protecting-workers'-health. Accessed November 12, 2019
- Skillgate E, Vingård E, Josephson M, Holm LW, Alfredsson L. Is smoking and alcohol consumption associated with long-term sick leave due to unspecific back or neck pain among employees in the public sector? Results of a three-year follow-up cohort study. J Rehabil Med. 2009;41(7):550–556.
- Tsai SP, Bhojani FA, Wendt JK. Risk factors for illness absence due to musculoskeletal disorders in a 4-year prospective study of a petroleummanufacturing population. J Occup Environ Med. 2011;53(4):434–440.
- Inoue-Choi M, Liao LM, Reyes-Guzman C, Hartge P, Caporaso N, Freedman ND. Association of long-term, low-intensity smoking with allcause and cause-specific mortality in the National Institutes of Health-AARP Diet and Health Study. JAMA Intern Med. 2017;177(1):87–95.
- Inoue-Choi M, Hartge P, Liao LM, Caporaso N, Freedman ND. Association between long-term low-intensity cigarette smoking and incidence of smoking-related cancer in the national institutes of health-AARP cohort. *Int J Cancer.* 2018;142(2):271–280.
- Cairney P, Yamazaki M. A comparison of tobacco policy in the UK and Japan: if the scientific evidence is identical, why is there a major difference in policy? J Comp Policy Anal Res Pract. 2018;20(3):253–268.
- Matayoshi T, Tabuchi T, Gohma I, Shimizu T. Tobacco and noncommunicable diseases control in Japan. Circ J. 2018;82(12):2941–2942.
- Akter S, Nakagawa T, Honda T, et al.; Japan Epidemiology Collaboration on Occupational Health Study Group. Smoking, smoking cessation, and risk of mortality in a Japanese working population—Japan epidemiology collaboration on occupational health study. Circ J. 2018:82(12):3005–3012.
- Nishiura C, Nanri A, Kashino I, et al. Age-, sex-, and diagnosis-specific incidence rate of medically certified long-term sick leave among private sector employees: the Japan Epidemiology Collaboration on Occupational Health (J-ECOH) study. J Epidemiol. 2017;27(12):590–595.
- Quist HG, Thomsen BL, Christensen U, et al. Influence of lifestyle factors on long-term sickness absence among female healthcare workers: a prospective cohort study. BMC Public Health. 2014;14:1084.
- Vingård E, Lindberg P, Josephson M, et al. Long-term sick-listing among women in the public sector and its associations with age, social situation, lifestyle, and work factors: a three-year follow-up study. Scand J Public Health. 2005;33(5):370–375.
- Christensen KB, Lund T, Labriola M, Bültmann U, Villadsen E. The impact of health behaviour on long term sickness absence: results from DWECS/ DREAM. *Ind Health*. 2007;45(2):348–351.
- Saha SP, Bhalla DK, Whayne TF Jr, Gairola C. Cigarette smoke and adverse health effects: an overview of research trends and future needs. *Int J Angiol.* 2007;16(3):77–83.
- Dong XS, Wang X, Largay JA. Occupational and non-occupational factors associated with work-related injuries among construction workers in the USA. Int J Occup Environ Health. 2015;21(2):142–150.
- Chau N, Bourgkard E, Bhattacherjee A, Ravaud JF, Choquet M, Mur JM; Lorhandicap Group. Associations of job, living conditions and lifestyle with occupational injury in working population: a population-based study. Int Arch Occup Environ Health. 2008;81(4):379–389.
- Nakata A, Ikeda T, Takahashi M, et al. The prevalence and correlates of occupational injuries in small-scale manufacturing enterprises. J Occup Health. 2006;48(5):366–376.
- Nakata A, Ikeda T, Takahashi M, et al. Non-fatal occupational injury among active and passive smokers in small- and medium-scale manufacturing enterprises in Japan. Soc Sci Med. 2006;63(9):2452–2463.

- Wen CP, Tsai SP, Cheng TY, Chan HT, Chung WS, Chen CJ. Excess injury mortality among smokers: a neglected tobacco hazard. *Tob Control*. 2005;14 (Suppl 1):i28–i32.
- 24. Hiscock R, Bauld L, Amos A, Fidler JA, Munafò M. Socioeconomic status and smoking: a review. *Ann NY Acad Sci.* 2012;1248:107–123.
- Cubbin C, LeClere FB, Smith GS. Socioeconomic status and injury mortality: individual and neighbourhood determinants. J Epidemiol Community Health. 2000;54(7):517–524.
- 26. Turner C, McClure R, Pirozzo S. Injury and risk-taking behavior-a systematic review. *Accid Anal Prev.* 2004;36(1):93–101.
- McClernon FJ, Kollins SH. ADHD and smoking: from genes to brain to behavior. Ann NY Acad Sci. 2008;1141:131–147.
- 28. Chien WC, Chung CH, Lin FH, et al. The risk of injury in adults with attention-deficit hyperactivity disorder: a nationwide, matchedcohort, population-based study in Taiwan. Res Dev Disabil. 2017;65:57-73.
- Ferrie JE, Head J, Shipley MJ, Vahtera J, Marmot MG, Kivimäki M. BMI, obesity, and sickness absence in the Whitehall II study. Obesity (Silver Spring). 2007;15(6):1554–1564.

- US Department of Health and Human Services. The Health Consequences of Smoking—50 Years of Progress: A Report of the Surgeon General. Atlanta: 2014
- Honjo K, Iso H, Tsugane S, et al. The effects of smoking and smoking cessation on mortality from cardiovascular disease among Japanese: pooled analysis of three large-scale cohort studies in Japan. *Tob Control*. 2010;19(1):50–57.
- Hackshaw A, Morris JK, Boniface S, Tang JL, Milenković D. Low cigarette consumption and risk of coronary heart disease and stroke: meta-analysis of 141 cohort studies in 55 study reports. BMJ. 2018;360:j5855.
- Fluharty M, Taylor AE, Grabski M, Munafò MR. The association of cigarette smoking with depression and anxiety: a systematic review. *Nicotine Tob Res.* 2017;19(1):3–13.
- Luger TM, Suls J, Vander Weg MW. How robust is the association between smoking and depression in adults? A meta-analysis using linear mixed-effects models. Addict Behav. 2014;39(10):1418–1429.
- Taylor AE, Fluharty ME, Bjørngaard JH, et al. Investigating the possible causal association of smoking with depression and anxiety using Mendelian randomisation meta-analysis: the CARTA consortium. BMJ Open. 2014;4(10):e006141.