

# BMI and Medically Certified Long-Term Sickness Absence Among Japanese Employees

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**Objective:** In contrast to the association between excess weight and sickness absence (SA), the association in relation to underweight has been under-researched. This study aimed to examine the effects of BMI at both extremes of its distribution on SA.

**Methods:** Data came from the Japan Epidemiology Collaboration on Occupational Health study of 77,760 workers aged 20 to 59 years (66,166 males, 11,594 females). Information was collected on medically certified long-term SA (LTSA) (i.e., SA lasting  $\geq 30$  consecutive days) from April 2012 to March 2017. A sex-specific Cox proportional hazards model was used to investigate the associations.

**Results:** Among males, both obesity (hazard ratio [HR]=1.81, 95% CI: 1.50-2.17) and underweight (HR=1.56, 95% CI: 1.23-1.96) were significantly associated with LTSA compared with normal weight. This U-shaped association between BMI categories and LTSA was observed both for mental and physical disorders. Among females, an elevated risk was observed among those with overweight (HR=1.54, 95% CI: 1.16-2.05).

**Conclusions:** In a cohort of the Japanese working-age population, both obesity and underweight were associated with a greater risk of LTSA in males. Future research should not overlook the excess risk of LTSA associated with underweight.

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## Introduction

A growing body of literature has focused on sickness absence (SA), defined here as absence from work because of health-related problems, given its large costs imposed on society, which include direct (e.g., medical expenditures) and indirect (e.g., decreased work productivity, social insurance claims) costs (1-3). The World Health

Organization estimated that work-related health problems contributed to an economic loss of 4% to 6% of gross domestic product for most countries (4).

Several studies have reported an increase in the risk of SA associated with excess weight (5-11). For example, a systematic review of 36 studies by Neovius et al. (6) concluded that obesity increases the risk of SA,

## Study Importance

### What is already known?

- ▶ A large body of literature has reported the association between excess weight and sickness absence, although little attempt has been made to examine the association between underweight and sickness absence.

### What does this study add?

- ▶ Underweight is associated with a greater risk of medically certified long-term sickness absence in Japanese males. Consistent with previous research, obesity is positively associated with sickness absence.
- ▶ Future research should not overlook excess risk of sickness absence associated with underweight as well as excess weight.

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albeit with different definitions in terms of duration of SA, data source (self-report vs. objectively recorded), and causes of SA (all-cause vs. cause-specific). More recently, Neovius et al. (7) showed by using a Swedish nationwide cohort that obesity was associated with a 13%, 35%, and 34% increase in risk for short-term (i.e.,  $\leq 7$  days), intermediate-term (i.e., 8-30 days), and long-term SA (LTSA) (i.e.,  $> 30$  days), respectively, compared with normal weight.

Some important issues remain to be addressed. First, in contrast to the extensive research on the association between excess weight and SA, the association in relation to underweight has been under-researched, and the results are inconsistent (7,9,11,12). This might be an important omission in our knowledge, particularly in non-Western settings, where obesity prevalence is not as high as those reported in high-income Western countries (13). In Japan, for example, the prevalence of adult underweight is 3.5% for males and 9.3% for females among the general population (13), and the corresponding figures were 3.5% and 14.6% among a working-age population (14). In addition, underweight has been linked with several negative health outcomes in Japan (15,16). Second, several previous studies (as reviewed in Neovius et al.) (6) used self-reported information on SA and/or BMI, which is subject to recall bias. Third, evidence is scarce on the relationship between BMI categories and cause-specific SA; identifying specific causes of SA may help us understand underlying pathways linking BMI categories and SA (17,18).

To address these issues, we examined the association between BMI, which is calculated based on measured height and weight, and the incidence of medically certified LTSA episodes (i.e., SA lasting  $\geq 30$  consecutive days) by using data collected in the Japan Epidemiology Collaboration on Occupational Health (J-ECOH) study. Furthermore, we paid special attention to the effect of BMI at both ends of the distribution (i.e., underweight and excess weight).

## Methods

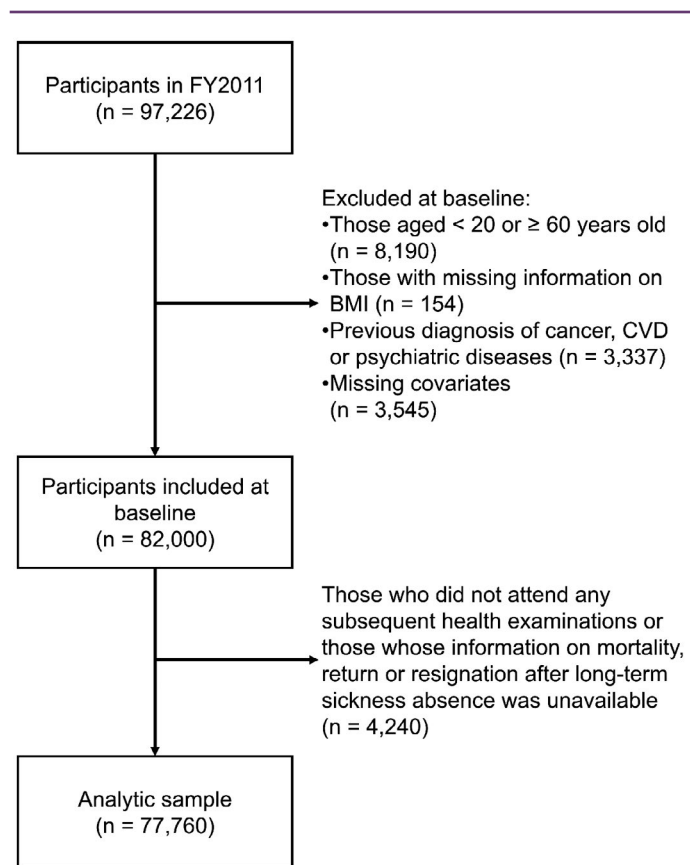
### Design of J-ECOH study

J-ECOH is an ongoing epidemiological survey investigating health determinants among Japanese workers across various industry sectors (e.g., electric machinery and apparatus manufacturing, steel, chemical, gas, nonferrous metal manufacturing, automobile and instrument manufacturing, plastic product manufacturing, health care). In Japan, employers must organize general health examinations for their employees at least once a year under the Industrial Safety and Health Act; we collected anthropometric and biochemical data as well as information on medical history and some lifestyle parameters in these health examinations.

The study protocol was approved by the Ethics Committee of the National Center for Global Health and Medicine, Japan. While the participants did not provide verbal or written informed consent to join the study, they were allowed to refuse to participate in the study at any time. This procedure conformed to the Japanese Ethical Guidelines for Epidemiological Research, which facilitate the procedure for obtaining consent in observational studies that use existing data. All data were analyzed anonymously.

### Analytic cohort

As shown in Figure 1, out of 97,226 workers who participated in the health checkup in Fiscal Year 2011, we excluded those who were younger than 20 years old and those who were 60 years old or older ( $n=8,190$ ); those who did not provide information on BMI ( $n=154$ );



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

those with a history of cancer, cardiovascular disease (CVD), or mental disorders ( $n=3,337$ ) to avoid reverse causality (i.e., those with previous diagnosis of such disorders might have lost their weight); and those with missing information on covariates ( $n=3,545$ ). We further excluded those who did not attend any subsequent health examinations and those whose information on mortality, return, or resignation after long-term sick leave was unavailable ( $n=4,240$ ). Consequently, we had an analytic sample of 77,760 (66,166 males and 11,594 females).

### Follow-up

A study-specific registry was created in April 2012 to collect information on LTSA, cardiovascular events (i.e., myocardial infarction and stroke), and death. Information collected in the annual health checkups throughout the study period was also obtained. These data were used to follow study participants and determine the type and date of events they experienced. If no such events were recorded, participants were considered to be under observation until the date of the last health checkup.

### Outcome

The outcome was the onset of LTSA during the period between April 1, 2012, and March 31, 2017. Information on specific diagnoses for LTSA was also obtained from medical certificates endorsed by primary doctors; these certificates were submitted by the employees to their companies to apply for paid sick leave. We then coded the diagnoses based on the *International Classification of Diseases, 10th Revision (ICD-10)*.

We classified all the LTSA episodes into LTSA because of mental and behavioral disorders (ICD code: F00-F99), LTSA because of injuries or external causes (S00-T98), and LTSA because of physical disorders (i.e., LTSA episodes other than specified above). For the physical disorders, we further examined the association between BMI categories and LTSA because of cancer (C00-C97 and D00-D48), LTSA because of CVD (I60-I69 and I20-I25), and LTSA because of musculoskeletal diseases (M00-M99).

### Explanatory variable

Body height and weight were measured by using a scale; weight was measured in light clothes and without shoes. BMI was calculated as weight (kilograms) divided by height (meters squared), which was then categorized into the following categories: <18.5, 18.5 to 24.9, 25.0 to 29.9, and ≥30.

### Covariates

Information was obtained on age (in years), sex, smoking status (currently smoke, quit, and never smoke), hypertension, diabetes, and dyslipidemia at the baseline. Participants were judged to be hypertensive if their systolic blood pressure was ≥140 mmHg, their diastolic blood pressure was ≥90 mmHg, or they took antihypertensive medication. Diabetes was defined as a fasting plasma glucose level ≥126 mg/dL (7.0 mmol/L), hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) ≥6.5% (48 mmol/mol), or the current use of antidiabetic medication. Plasma glucose was measured either by enzymatic method or glucose oxidase peroxidative electrode method. HbA<sub>1c</sub> was measured either by latex agglutination immunoassay, high-performance liquid chromatography (HPLC) method, or enzymatic method and was converted to the National Glycohemoglobin Standardization Program (NGSP) equivalent value (percent) by using the following formula: A<sub>1c</sub> (%) = 1.02 × A<sub>1c</sub> (%) based on the Japan Diabetes Society value) + 0.25. Dyslipidemia was defined as triglycerides ≥150 mg/dL (1.7 mmol/L), low-density lipoprotein cholesterol ≥140 mg/dL (3.6 mmol/L), high-density lipoprotein cholesterol <40 mg/dL (1.0 mmol/L), or taking antidyslipidemia medication.

### Statistical analysis

After confirming interaction between sex and BMI categories in relation to LSTA (i.e., a significant interaction between underweight and sex

[*P* = 0.007]), a sex-specific Cox proportional hazards regression analysis was used to investigate the association between BMI categories and medically certified LTSA. Person-time was calculated from March 31, 2012 (i.e., 1 day before the beginning of the study period), to the first day of LTSA, date of death, date of the last participation in the health examination, or the end of follow-up period (March 31, 2017), whichever occurred first. For the cause-specific analyses, those who took LTSA because of other diseases were also censored on the date of LTSA. We confirmed that there was no collinearity of independent variables.

We used several steps for statistical adjustment; Model 1 adjusted for age and smoking status, and Model 2 further adjusted for possible mediators (i.e., hypertension, diabetes, and dyslipidemia). The cause-specific analyses were conducted only among male participants because of insufficient sample size among female participants. In addition, to test the robustness of the study findings, we also conducted sensitivity analyses in which (1) we further excluded those with BMI of 15 or less or 40 or more (males: *n* = 115; females: *n* = 32); (2) we further excluded those who were aged 50 or older (males: *n* = 17,336; females: *n* = 2,234); and (3) we did not exclude those with a history of cancer, CVD, and psychiatric disorders at baseline.

All the statistical analyses were conducted using Stata version 15.0 (StataCorp, College Station, Texas). Proportional hazard assumption was tested using Schoenfeld's test, and we confirmed that there was no violation of the assumption. Results are shown in the form of hazard ratios (HR) with 95% CI. We also calculated *P* values for linear and quadratic trends, using coefficients of orthogonal polynomials (specifically, “contrast” command in Stata). Statistical significance was set at *P* < 0.05 (two-tailed).

### Results

During the period between April 2012 and March 2017, 1,686 males and 377 females had episodes of SA lasting a consecutive 30 days or longer, while 17,756 males and 3,847 females were censored during the period. As a result, we had a follow-up of 289,433 person-years for males and 48,651 person-years for females, and the incidence rate of LTSA per 1,000 person-years was 5.83 (95% CI: 5.55-6.11) for males and 7.75 (95% CI: 7.00-8.57) for females. Sex-specific survival curves are shown in Supporting Information Figure S1.

**TABLE 1** Baseline characteristics of study participants in the Japan Epidemiology Collaboration on Occupational Health (2011)

	All participants	Baseline BMI categories			
		<18.5	18.5-24.9	25.0-29.9	≥30.0
<b>Men</b>	( <i>n</i> = 66,166)	( <i>n</i> = 2,304)	( <i>n</i> = 44,883)	( <i>n</i> = 15,865)	( <i>n</i> = 3,114)
Age, mean (SD)	41.8 (10.3)	37.2 (11.2)	41.5 (10.5)	43.5 (9.5)	40.7 (9.4)
Smoking, <i>n</i> (%)	25,213 (38.1)	1,041 (45.2)	16,623 (37.0)	6,192 (39.0)	1,357 (43.6)
Hypertension, <i>n</i> (%)	12,393 (18.7)	144 (6.3)	6,142 (13.7)	4,657 (29.4)	1,450 (46.6)
Diabetes, <i>n</i> (%)	9,353 (14.1)	363 (15.8)	5,452 (12.1)	2,577 (16.2)	961 (30.9)
Dyslipidemia, <i>n</i> (%)	28,488 (43.1)	282 (12.2)	16,282 (36.3)	9,804 (61.8)	2,120 (68.1)
<b>Women</b>	( <i>n</i> = 11,594)	( <i>n</i> = 1,793)	( <i>n</i> = 8,103)	( <i>n</i> = 1,278)	( <i>n</i> = 420)
Age, mean (SD)	40.3 (9.7)	38.0 (9.5)	40.2 (9.7)	42.7 (9.5)	42.6 (8.7)
Smoking, <i>n</i> (%)	1,297 (11.2)	195 (10.9)	885 (10.9)	146 (11.4)	71 (16.9)
Hypertension, <i>n</i> (%)	1,044 (9.0)	60 (3.3)	566 (7.0)	257 (20.1)	161 (38.3)
Diabetes, <i>n</i> (%)	1,523 (13.1)	237 (13.2)	993 (12.3)	188 (14.7)	105 (25.0)
Dyslipidemia, <i>n</i> (%)	2,474 (21.3)	162 (9.0)	1,525 (18.8)	559 (43.7)	228 (54.3)

Table 1 shows baseline characteristics of the study participants stratified by sex and baseline BMI categories. Among men, those in their 30s and 40s were more likely to have obesity compared with those in their 20s and 50s. Participants in both underweight and obesity categories were more likely to be smokers compared with those in the normal weight category. The prevalence of hypertension, diabetes, and dyslipidemia was highest among the obesity category. Among women, obesity prevalence was higher when they were in their 30s and 40s compared with the other age categories. The prevalence of smoking, hypertension, diabetes, and dyslipidemia was highest among those in the obesity category.

Table 2 shows the number of participants who took LTSA, stratified by ICD-10 code. For mental and behavioral disorders, depressive episode and reaction to severe stress and adjustment disorders occupied more than three-quarters of LTSA episodes caused by mental and behavioral disorders, whereas neoplasms, diseases of the musculoskeletal system and connective tissue, and diseases of the circulatory system were the three major disease categories that contributed to LTSA caused by physical disorders. Fracture of lower leg was the largest contributor to LTSA caused by injuries or external causes.

As shown in Table 3, a Cox proportional hazards regression analysis among male participants exhibited a U-shaped association between BMI categories and LTSA; when we adjusted for age and smoking status (Model 1), those with BMI  $\geq 30$  had a risk of medically certified LTSA that was 1.81 times (95% CI: 1.50-2.17) higher compared with those with normal weight. Having underweight (BMI  $< 18.5$ ) was also associated with higher risk for LTSA (HR = 1.56; 95% CI: 1.23-1.96). These associations remained statistically significant after further adjusting for baseline hypertension, diabetes, and dyslipidemia; the HR for individuals with obesity and underweight was 1.47 (95% CI: 1.21-1.78) and 1.63 (95% CI: 1.29-2.05), respectively. Among female participants, Model 1 revealed a statistically significant increase in the risk for LSTA among those in the overweight category (HR = 1.54; 95% CI: 1.16-2.05) compared with those with normal weight, but this association was attenuated in Model 2 (HR = 1.31; 95% CI: 0.97-1.76). We did not find any increase in LSTA risk among those in the underweight and obesity categories.

In cause-specific analyses among male participants (Table 4), obesity and underweight were associated with a risk for LTSA that was 1.51 times (95% CI: 1.13-2.01) and 1.79 times (95% CI: 1.13-2.45) higher, respectively, because of mental disorders in the fully adjusted model. The physical disorders also showed a U-shaped association between BMI and LTSA; the HR for those with BMI  $\geq 30$  was 1.56 (95% CI: 1.18-2.07), and that for those with BMI  $< 18.5$  was 1.58 (95% CI: 1.08-2.31) in the fully adjusted model. There were no significant associations for LTSA because of CVD, cancer, and musculoskeletal disorders, except for an increased risk of LTSA because of CVD associated with obesity (Model 1; HR = 3.03; 95% CI: 1.53-6.00).

Sensitivity analyses showed no substantial changes in the results (Supporting Information Tables S1-S3). Specifically, we found U-shaped associations between BMI categories and LSTA among male participants, while no clear evidence was observed among female participants. In the analysis including those with a history of cancer, CVD, and psychiatric disorders at baseline, the HR for female participants with BMI  $\geq 30$  became statistically significant in Model 1. This may indicate that those who had a history of cancer, CVD, or psychiatric disorders tended to have obesity and take LTSA among female participants.

**TABLE 2** Participants who took LTSA in Japan Epidemiology Collaboration on Occupational Health Study, stratified by ICD-10 (those with at least 15 cases reported)

ICD	Description	Cases
<b>Mental and behavioral disorders</b>		
F32	Depressive episode	500
F43	Reaction to severe stress and adjustment disorders	161
F41	Other anxiety disorders	46
F45	Somatoform disorders	23
F48	Other neurotic disorders	20
F20	Schizophrenia	18
F31	Bipolar affective disorder	17
	Others	67
<b>Physical disorders</b>		
C00-D48	Neoplasms	313
M00-M99	Diseases of the musculoskeletal system and connective tissue	181
I00-I99	Diseases of the circulatory system	159
G00-G99	Diseases of the nervous system	73
000-099	Pregnancy, childbirth, and the puerperium	59
K00-K93	Diseases of the digestive system	58
H00-H59	Diseases of the eye and adnexa	32
E00-E90	Endocrine, nutritional, and metabolic diseases	25
J00-J99	Diseases of the respiratory system	20
N00-N99	Diseases of the genitourinary system	20
A00-B99	Certain infectious and parasitic diseases	19
L00-L99	Diseases of the skin and subcutaneous tissue	15
R00-R99	Symptoms, signs, and abnormal clinical and laboratory findings not elsewhere classified	15
	Others	16
<b>Injuries/external causes</b>		
S82	Fracture of lower leg, including ankle	48
S92	Fracture of foot, except ankle	16
S42	Fracture of shoulder and upper arm	15
S86	Injury of muscle and tendon at lower leg level	15
	Others	111

One individual did not provide information on cause of LTSA.

## Discussion

In this large working-age population in Japan, both obesity and underweight were associated with a higher risk for medically certified LTSA among male workers. This U-shaped association between BMI categories and LTSA was observed both for mental and physical disorders. Among females, an elevated risk was observed only for those in the overweight category. Our findings suggest the importance of future studies focusing on how both excess weight and underweight are linked with higher risk of LTSA. In addition, occupational physicians should provide health education for employees with lower BMI to help them



**TABLE 3** Adjusted HR and 95% CI for medically certified LTSA shown by baseline BMI categories among Japanese aged 20 to 59 years old (2012-2017)

	Baseline BMI categories				<i>P</i> <sub>linear</sub>	<i>P</i> <sub>quadratic</sub>
	<18.5	18.5-24.9	25.0-29.9	≥30.0		
<b>Male participants</b>	( <i>n</i> = 2,304)	( <i>n</i> = 44,883)	( <i>n</i> = 15,865)	( <i>n</i> = 3,114)		
<i>n</i> events	78	1,024	455	129		
Person-years	10,059	196,849	68,862	13,663		
Model 1	1.56 (1.23-1.96)	ref.	1.22 (1.09-1.36)	1.81 (1.50-2.17)	<0.001	<0.001
Model 2	1.63 (1.29-2.05)	ref.	1.11 (0.99-1.24)	1.47 (1.21-1.78)	0.08	<0.001
<b>Female participants</b>	( <i>n</i> = 1,793)	( <i>n</i> = 8,103)	( <i>n</i> = 1,278)	( <i>n</i> = 420)		
<i>n</i> events	49	255	58	15		
Person-years	7,468	34,127	5,283	1,773		
Model 1	0.86 (0.63-1.16)	ref.	1.54 (1.16-2.05)	1.20 (0.71-2.02)	0.01	0.79
Model 2	0.89 (0.66-1.22)	ref.	1.31 (0.97-1.76)	0.86 (0.50-1.49)	0.31	0.41

Models adjusted for age, sex, and smoking status at baseline (Model 1), baseline hypertension, diabetes, and dyslipidemia (Model 2).

**TABLE 4** Cause-specific analyses for medically certified LTSA shown by baseline BMI categories among Japanese males aged 20 to 59 years old (2012-2017)

	Baseline BMI categories				<i>P</i> <sub>linear</sub>	<i>P</i> <sub>quadratic</sub>
	<18.5	18.5-24.9	25.0-29.9	≥30.0		
<b>Person-years</b>	10,059	196,849	68,862	13,663		
<b>1. Sick leave due to mental disorders</b>						
<i>n</i> events	44	453	188	58		
Model 1	1.70 (1.25-2.32)	ref.	1.23 (1.04-1.46)	1.75 (1.33-2.30)	0.01	<0.001
Model 2	1.79 (1.31-2.45)	ref.	1.13 (0.95-1.35)	1.51 (1.13-2.01)	0.21	<0.001
<b>2. Sick leave due to physical disorders</b>						
<i>n</i> events	29	463	225	63		
Model 1	1.51 (1.04-2.21)	ref.	1.24 (1.06-1.46)	2.04 (1.57-2.66)	<0.001	<0.001
Model 2	1.58 (1.08-2.31)	ref.	1.11 (0.94-1.31)	1.56 (1.18-2.07)	0.13	<0.001
<b>2a. Sick leave due to cancer</b>						
<i>n</i> events	5	155	73	11		
Model 1	0.83 (0.34-2.04)	ref.	1.18 (0.89-1.56)	1.15 (0.62-2.13)	0.25	0.72
Model 2	0.83 (0.34-2.03)	ref.	1.15 (0.86-1.53)	1.05 (0.56-1.98)	0.41	0.63
<b>2b. Sick leave due to cardiovascular diseases</b>						
<i>n</i> events	2	51	35	10		
Model 1	1.00 (0.24-4.10)	ref.	1.68 (1.09-2.58)	3.03 (1.53-6.00)	0.002	0.47
Model 2	1.23 (0.30-5.12)	ref.	1.28 (0.82-2.00)	1.71 (0.83-3.53)	0.23	0.53
<b>2c. Sick leave due to musculoskeletal diseases</b>						
<i>n</i> events	6	90	35	11		
Model 1	1.53 (0.67-3.52)	ref.	1.02 (0.69-1.51)	1.80 (0.96-3.37)	0.51	0.07
Model 2	1.51 (0.66-3.48)	ref.	1.00 (0.67-1.51)	1.68 (0.86-3.26)	0.65	0.09
<b>3. Sick leave due to injuries/external causes</b>						
<i>n</i> events	5	108	42	8		
Model 1	0.97 (0.39-2.38)	ref.	1.05 (0.73-1.50)	1.08 (0.53-2.22)	0.75	0.99
Model 2	0.99 (0.40-2.45)	ref.	0.99 (0.68-1.43)	0.95 (0.45-2.01)	0.91	0.95

Data presented as adjusted HR and 95% CI. Models adjusted for age, sex, and smoking status at baseline (Model 1), baseline hypertension, diabetes, and dyslipidemia (Model 2).

achieve a healthy body weight as well focusing on weight loss among those with excess body weight.

### Obesity and LTSA among male participants

The present findings of an increased risk of LTSA associated with obesity in men are in line with those reported in previous studies (5-9,11,19-21). The effect size observed in our study (i.e., HR=1.47-1.81) was more or less equivalent to those reported in previous studies on LTSA (i.e., sick leave lasting for approximately 30 days or longer). For example, Neovius et al. (7) reported that obesity was linked with an HR of 1.34 for LTSA among the male general population in Sweden who performed mandatory military conscription tests (which included the measurement of height and weight) in 1969 to 1970 and who were followed up during the period between 1986 and 2005. Vingård et al. (21) reported that obesity was associated with higher risks for sick-listing  $\geq 28$  days compared with normal weight among Swedish public sector female employees (relative risk [RR] = 1.3).

We are not aware of any previous studies that conducted cause-specific analyses on the association between obesity and LTSA, yet our finding of an increased risk of LTSA because of mental disorders among those with BMI  $\geq 30$  is in line with previous studies that investigated the association between obesity and mental disorders in general (22,23). For example, in their systematic review, Luppino et al. (22) showed an increase in the risk for depression associated with overweight (odds ratio [OR]=1.27) and obesity (OR=1.55). In addition, using information collected in 14 cross-sectional studies, Garipey et al. (23) reported that obesity was associated with higher odds for anxiety disorders (OR = 1.4). It is possible that obesity leads to a worsening of mental health via stigmatization (24), lower self-esteem (25), altered adipose-related metabolic signals (26,27), and worse health conditions (28), which may result in the development of mental disorders.

Our findings that obesity was associated with an increased risk of LTSA because of physical disorders, which were largely caused by noncommunicable diseases in this study, accord with a large body of literature showing that obesity is a major risk factor for noncommunicable diseases (28). LTSA because of CVD was the only outcome with which we found a significantly higher risk among those with BMI  $\geq 30$  in the cause-specific analysis (Model 1); while previous studies have not specifically focused on the association between obesity and LTSA because of CVD, this finding is in line with Virtanen et al. (10), who investigated the association between overweight and obesity and the total number of SA days per year because of circulatory diseases (overweight: RR=1.16; obesity: RR=1.82). In addition, it accords with several previous studies that examined the association between obesity and CVD-related morbidity and mortality (15,29). Given that the observed association was largely attenuated after adjusting for hypertension, diabetes, and dyslipidemia, these cardiometabolic markers might underlie the association between obesity and LTSA because of CVD; a meta-analysis using information collected in 97 prospective cohort studies also suggested these markers as possible mechanisms linking overweight and obesity and CVD (30).

We did not find evidence of significant associations in relation to LTSA because of cancer or LSTA because of musculoskeletal disorders. Albeit with differences in the outcomes studied, this finding seems to contradict with those reported in previous studies on the association of obesity with the incidence of cancer (31) and with the incidence

of musculoskeletal disorders (32-35). One possible interpretation for such discrepancy might have been due to our definition of SA (i.e., SA  $\geq 30$  consecutive days). For example, a report by the Ministry of Health, Labour and Welfare in Japan (36) showed that the average number of hospitalization days because of cancer decreased from 35.8 days in 1996 to 18.7 days in 2014; this indicates that excess risk of cancer associated with obesity may not be sufficiently captured by our SA definition. Based on data on SA lasting longer than 9 days in four European cohorts, Virtanen et al. (10) showed that obesity was positively associated with the total number of SA days per year because of musculoskeletal diseases (RR=1.59). These findings suggest that the effect of excess weight on SA may differ depending on the duration of SA used to define the outcome.

### Underweight and LTSA among male participants

Our finding is in line with Quist et al. (9), who showed that a 1-kg/m<sup>2</sup> decrease in BMI below 18.5 was associated with a 32% increased risk for LTSA (defined as  $\geq 3$  consecutive weeks of registered SA) among female health care workers in Denmark, while Neovius et al. (7) did not find any evidence of association between underweight and LTSA (i.e., SA  $> 30$  days) among Swedish males. More studies are needed to confirm whether the association between underweight and LTSA observed in our study also exists in Western countries despite the difference in social norms (e.g., working hours, work-life balance, gender imbalance at workplace) (37). It should also be mentioned that previous studies on the association between underweight and SA of any duration reported conflicting results (positive association, inverse association, and no association) (7,11,12,38), which warrants further investigation.

As illustrated in our cause-specific analysis, underweight was linked with elevated risk for LSTA because of both mental and physical disorders. While we are not aware of any previous studies on the cause-specific association between underweight and LTSA, our finding in relation to mental disorders is in line with a review by Jung et al. (39), who concluded that underweight was associated with an increased risk for subsequent depression. The elevated risk for physical disorders associated with underweight also was previously reported in the Japanese population (15,16), as well as in the other countries (40,41). It is also possible that the observed association between underweight and LTSA might have been caused by some health conditions on which we did not collect information at baseline (e.g., eating disorders, autoimmune disease). Future studies should not overlook the excess risk of SA associated with underweight.

### BMI categories and LTSA among females

The association between BMI categories and LTSA was not clear among female participants; those in the overweight category, but not those in the obesity or underweight categories, were at a higher risk for LTSA compared with those with normal weight. This is somewhat unexpected given that existing data showed a U-shaped association between BMI and morbidity or mortality in both males and females (42).

The nonsignificant association in relation to obesity among females might have been due to the limited number of participants classified into the obesity category in this study; there were only 15 participants who were in the obesity category and took LTSA out of 420 participants in the same category. This might have limited our statistical power. In fact, when overweight and obesity categories were combined, the HR

for LTSA was 1.45 (95% CI: 1.12-1.89) in Model 1, which was attenuated and became nonsignificant in Model 2 (HR = 1.19; 95% CI: 0.90-1.58). These findings suggest that the excess risk for LTSA among the Japanese female working population may become evident even in the overweight category.

Given the number of the participants in the underweight category deemed sufficient, low statistical power may not be a reason for the null finding on underweight. It is possible that our female study participants do not represent the working-age female population in Japan. For example, underweight prevalence in this population (15.5%) is generally higher than those estimated previously for Japanese females of working age in 2011 (ranging from 5.7% [50-54 years old] to 15.4% [20-24 years old]) (13). In addition, female labor participation in Japan is lower than the The Organisation for Economic Co-operation and Development average (43), and the situation is worse in large-scaled corporations, as exemplified by the low proportion of female participants in this study. In turn, those females who participated in the survey might have been a result of survival effects (e.g., positive health selection). Our findings for females might be different from what we would have obtained if we recruited females of all age groups.

## Strengths and limitations

This study has several strengths. First, we examined the association between underweight and LTSA, which has been little studied compared with the association between excess weight and LTSA. Second, we obtained information on measured height and weight to compute BMI and medically certified LTSA episodes to define the outcome. Third, we used a large data set to examine the association between BMI categories and LTSA, which enabled us to conduct cause-specific analyses. Fourth, we used information collected in the health examinations, which are mandatory under the Industrial Safety and Health Act; the participation rate was high, and thus the study findings were less likely to have been affected by participant attrition.

There are also several limitations to this study that should be addressed. First, we did not include SA less than 30 days; we did not account for the effect of BMI categories on SA caused by minor health problems (e.g., general cold). While our intention was to aim at investigating the effect of BMI on severer forms of SA, results may be different when we include SA of any duration. Second, older individuals, that is, those who were supposed to retire soon, might not have been able to take LTSA; while we confirmed that the results did not change when our analysis confined the participants to those aged less than 50 years, such a ceiling effect might have biased the results. Last, our study participants might not have been fully representative of the Japanese working-age population. Our study participants were collected at 12 work sites in the Japanese private sector and did not include other professions, those who work in small business, or those who engage in a part-time job. Caution should be made in generalizing the findings.

## Conclusion

Among the Japanese working-age population, both obesity and underweight were positively associated with a higher risk for medically certified LTSA in males. These associations were observed when we conducted cause-specific analyses in relation to mental disorders and physical disorders and deemed robust. Future studies should not

overlook excess risk of SA associated with underweight as well as excess weight. **O**

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**Supporting information:** Additional Supporting Information may be found in the online version of this article.

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