Introduction

A recent survey report prepared by the Ministry of Health, Labour, and Welfare (MHLW) on the current health status in Japan stated that “lifestyle-related diseases account for about 60% of all mortalities and about 30% of all medical costs” [1]. There has been an increase in the number of patients with lifestyle-related diseases, such as diabetes mellitus (DM). The 2007 National Health and Nutrition Survey published sobering data showing that 8.9 million people were strongly suspected of having DM and potentially 13.2 million people had DM. More than 10 years have passed since that survey, but the 2017 National Health and Nutrition Survey results showed no significant changes in the data [2].

In this context, Health Japan 21 (second term) has set “achieving extension of healthy life expectancy and reduction of health disparities” as its ultimate goal, which also includes “thorough prevention of the onset and progression of lifestyle-related diseases” in its basic health promotion policies. As part of those efforts,

Work Environment-related Stress Factors are Correlated with Diabetes Development in Workers with Impaired Glucose Tolerance: A 5-year Follow-up Study Using the Brief Job Stress Questionnaire (BJSQ)

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Abstract: Several previous studies have investigated the effects of occupational stress on the onset of diabetes mellitus (DM), but there are few studies of occupational stress and DM using the Brief Job Stress Questionnaire (BJSQ), a standard stress check method in Japan. This study aimed to determine the relationship between occupational stress factors and the onset of DM using the BJSQ. We examined 6,620 male company workers aged 40 years and above in 2013, using the BJSQ. Overall, 2,604 subjects with impaired glucose tolerance who were free of mental disorders and DM were followed-up for 5 years and re-examined in 2017. A retrospective data analysis was conducted in 2019. We documented 241 new cases of DM in 2017 (diabetes group). Compared with the non-diabetes group, the subjects in the diabetes group had significantly decreased “skill utilization”. A binomial logistic regression analysis (generalized linear model) revealed that “skill utilization” was associated with the risk of DM development in 2017 (odds ratio, 1.632; 95% confidence interval, 1.061–2.510). Our results showed that low skill utilization might increase the risk of diabetes development in Japanese male workers.

Keywords: occupational stress, Brief Job Stress Questionnaire (BJSQ), diabetogenic factor, type 2 diabetes mellitus.

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the Japanese government launched specific health checkups and specific health guidance in 2008 to prevent lifestyle-related diseases, especially in people aged 40 years and older. These measures target a large portion of working-age population and are therefore crucial in the field of occupational health.

Equally important are mental health measures. According to surveys conducted by the MHLW, the percentage of workers with intense work-related stress was 50.6% in 1982, reached 62.8% in 1997, and has since remained around 60% [3]. Under these social circumstances, the Occupational Safety & Health Program formulated by the MHLW has specified mental health measures as a priority for the past 10 years [4].

Occupational health physicians in Japan are involved in the health management of workers, wherein they provide comprehensive medical care, including measures against lifestyle-related diseases and mental health impairments. In some cases, however, workers do not make an effort to improve their lifestyle habits due to stress, despite receiving health guidance about DM. As there have been several cases involving workers in high-stress environments who later developed early signs of DM, it is reasonable to assume that occupational stress may play a role in the onset of DM.

Several previous studies have investigated the effects of occupational stress on the onset of DM. A cross-sectional study of Swedish middle-aged women using the Karasek Job Content Questionnaire showed that low decision latitude increases the risk of DM [5]. A cohort study of British middle-aged men and women using the same questionnaire showed that job strain (high job demands/low job control) increases the risk of DM in obese women [6]. Another cohort study of German industrial male and female workers using the Siegrist Effort-Reward Imbalance Questionnaire showed that a high effort-reward imbalance increases the risk of DM and prediabetes in men [7].

The Brief Job Stress Questionnaire (BJSQ) [8], a product of a Grant-in-Aid for Scientific Research, is a standard stress check method in Japan. A cross-sectional study aimed to determine the relationship between components of metabolic syndrome and job strain using the BJSQ [9], but there are few studies of occupational stress and DM using the BJSQ. Therefore, here we used the BJSQ to conduct a longitudinal study of occupational stressors associated with the development of DM in workers.

Materials and Methods

Study sample

Among 6,620 male company workers aged 40 years or older who underwent routine annual health checkups and a stress check at work in 2013, 2,650 men with impaired glucose tolerance (IGT) did not meet the definition of DM. After excluding 46 men with mental disorders, the remaining 2,604 men were included in this study. IGT was defined as a hemoglobin A1c (HbA1c) level ≥5.6%, and DM was defined as an HbA1c level ≥6.5% or use of antidiabetic drugs (Figure 1).

Measurements

Parameters related to glucose and lipids were examined during the annual health checkups in 2013. A self-reported medical questionnaire was also used to assess past histories of mental disorders and DM, lifestyle habits (sleep time, smoking status, number of cigarettes smoked, alcohol drinking status, amount of alcohol consumption, exercise status, and hobbies), and work environment (occupation, overtime hours per month, and night work status).

For the stress check, we used the BJSQ to investigate job stressors (9 subscales, 17 items), stress responses (6 subscales, 29 items), and modifiers (4 subscales, 11 items). Scores for each of the subscale items on the stress check were calculated to obtain raw scores, which were then converted to a 5-point scale or standardized scores for evaluation. Higher scores indicated lower stress levels [8].

Glucose- and lipid-related data of the 2,604 subjects were used in the annual health checkups conducted in 2017 (4 years after the 2013 stress check). Subjects with an HbA1c level ≥5.6% were defined as having IGT, and those with an HbA1c level ≥6.5% or using antidiabetic drugs were defined as having DM. The primary goal was to find any correlations between the results of the 2013 health checkup and stressors and the onset of DM by 2017. A retrospective data analysis was conducted in 2019.

The study protocol was approved by the Ethics committee on medical research, University of Occu-
pational and Environmental Health (date of approval: July 11, 2019; approval No: R1-012).

Statistical analysis
Continuous variables were expressed as mean (standard deviation). The $\chi^2$ (chi-squared) test, Wilcoxon signed-rank test or Mann-Whitney U test was used for comparison between the two groups. Using binomial logistic regression analysis (generalized linear model), we calculated the odds ratios and 95% confidence intervals (CIs) to determine the risk factors of the BJSQ for the onset of DM in 2017. The model was produced by forward selection after using the Spearman’s rank correlation coefficient to remove factors with multicollinearity from the factors with $P$ values <0.25 in univariate analysis of health checkup results and job stressors in 2013. The significance level was set at $P <0.05$. Missing data were excluded from the analysis. IBM SPSS Statistics for Windows (Version 22.0. Armonk, NY: IBM Corp.) was used for statistical analysis.

Results

Clinical background in 2013
The mean age of the 2,604 subjects was 55.7 (7.8) years; body mass index (BMI) was 24.5 (3.5) kg/m$^2$; systolic blood pressure (SBP) was 135 (17) mmHg; diastolic blood pressure (DBP) was 82 (12) mmHg; high-density lipoprotein (HDL) cholesterol level was 56.9 (14.4) mg/dl; triglyceride (TG) level was 165.9 (128.9) mg/dl; low-density lipoprotein (LDL) cholesterol level was 124.2 (29.6) mg/dl; HbA1c level was 5.8 (0.2%); percentage of smokers was 35.8%; number of cigarettes smoked/day was 18 (7); alcohol consumption rate was 63.6%; estimated amount of alcohol consumed at one time was 1.7 (0.9) go (1 go = 180 ml of sake = 20 g of alcohol); percentage of individuals who exercised daily was 71.1%; estimated sleep time was 6.2 (0.9) hours; estimated monthly overtime work was 12.4 (11.1) hours; and percentage of night workers was 59.0%. By occupation, the subjects consisted of: field managers, 21.2%; office managers, 16.2%; station staff, 13.9%; rolling stock staff, 12.8%; office staff, 11.6%; drivers, 7.8%; track and structure staff, 5.5%; conductors, 4.0%; electrical engineering staff, 3.3%; secondees, 2.1%; research engineers, 0.6%; medical staff, 0.6%; and executives, 0.4%.

Effects of background factors on the onset of DM in 2017
Of the 2,604 subjects assessed in 2013, 241 were found to have developed DM in the 2017 health check-up.
up. There were no significant differences (all \( P > 0.05 \)) between those who developed DM in 2017 (new-onset DM cases) (n = 241) and the subjects in the non-DM group (n = 2,363) at the time of the 2013 health check-ups with regard to age; BMI; SBP; DBP; levels of HDL cholesterol, TG, LDL cholesterol, and HbA1c; lifestyle habits, and work environment (Table 1). In terms of stress assessment, the standardized scores of “skill utilization” in 2013 were significantly lower (\( P = 0.017 \), implying significantly higher stress levels) in the new-onset DM group than in the non-DM group (Table 2). This indicates the number of participants for whom there were effective BJSQ data in 2013 (Table 3).

To identify the risk factors in the BJSQ for DM development, several 2013 factors that could have contributed to the development of DM in 2017 were in-

| Table 1. Clinical background in 2013 according to the presence or absence of diabetes mellitus (DM) in 2017 |
|-----------------------------------------------|
| (2017 DM (+)) | (2017 DM (-)) | Significance Probability |
|----------------|----------------|-------------------------|
| Age (years)    | 56.5(7.1)      | 55.6(7.8)               | 0.169                |
| BMI (kg/m²)    | 24.7(3.5)      | 24.5(3.5)               | 0.517                |
| SBP (mmHg)     | 134.7(16.4)    | 134.7(17.2)             | 0.513                |
| DBP (mmHg)     | 81.6(12.4)     | 82.0(12.0)              | 0.997                |
| HDL (mg/dl)    | 57.6(16.1)     | 56.8(14.3)              | 0.541                |
| TG (mg/dl)     | 166.6(127.1)   | 165.9(129.1)            | 0.944                |
| LDL (mg/dl)    | 125.6(28.5)    | 124.1(29.7)             | 0.407                |
| HbA1c (%)      | 5.8(0.2)       | 5.8(0.2)                | 0.136                |
| Taking an antihypertensive (%)             | 14.1           | 14.3                    | 0.938                |
| Taking an antihyperlipidemic (%)           | 5.4            | 8.9                     | 0.064                |
| Lifestyle habits                               |
| Sleep time (hours)                           | 6.3(1.0)       | 6.2(0.9)                | 0.224                |
| Smoking rate (%)                             | 32.8           | 36.1                    | 0.300                |
| Cigarettes per day                           | 18.8(6.4)      | 18.1(6.7)               | 0.227                |
| Drinking rate (%)                            | 68.0           | 63.1                    | 0.131                |
| Alcohol consumptionc                         | 1.8(1.0)       | 1.7(0.9)                | 0.531                |
| Exercise rate (%)                            | 38.2           | 36.9                    | 0.687                |
| Having a hobby (%)                           | 69.3           | 71.3                    | 0.511                |
| Work environment                              |
| Monthly overtime (hours)                     | 12.9(11.4)     | 12.3(11.1)              | 0.700                |
| Night worker (%)                             | 62.5           | 58.6                    | 0.247                |
| Occupation                                    |
| Executive (%)                                | 10.0           | 90.0                    |
| Office manager (%)                           | 8.3            | 91.7                    |
| Research engineer (%)                        | 21.4           | 78.6                    |
| Medical staff (%)                            | 0              | 100                     |
| Field manager (%)                            | 9.3            | 90.7                    |
| Office staff (%)                             | 8.4            | 91.6                    |
| Driver (%)                                   | 11.1           | 88.9                    | 0.117                |
| Conductor (%)                                | 13.3           | 86.7                    |
| Station staff (%)                            | 11.8           | 88.2                    |
| Rolling stock staff (%)                      | 6.4            | 93.6                    |
| Track and structure staff (%)                | 13.4           | 86.6                    |
| Electrical engineering staff (%)             | 7.5            | 92.5                    |
| Secondee (%)                                 | 10.9           | 89.1                    |

*: The values are mean (standard deviation).  
\( \chi^2 \): Mann-Whitney test, \( \chi^2 \) test.  
\( \chi^2 \): The amount consumed at one time.  
BMI: Body mass index, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, HDL: High density lipoprotein, TG: Triglyceride, LDL: Low-density lipoprotein cholesterol, HbA1c: Hemoglobin A1c
vestigated using binomial logistic regression analysis (generalized linear model). The results of the analysis showed an association between “skill utilization” and the risk of DM development in 2017 (odds ratio, 1.632; 95% confidence interval, 1.061–2.510) (Table 4).

We also calculated the “skill utilization” cutoff in 2013 using the receiver operating characteristic curve by the presence/absence of DM in 2017. Subjects with a standardized score ≤3 (1,967 men) were classified as the low skill utilization group, while those with a standardized score ≥4 (404 men) were classified as the high skill utilization group. The rate of development of DM in 2017 was significantly lower in the high skill utilization group versus the low skill utilization group (9.9% vs. 6.4%, respectively; \( P = 0.031 \)).

### Table 2. Stress check results in 2013 according to the presence or absence of diabetes mellitus (DM) in 2017

| Job stressors     | 2017 DM (+) n = 241 | 2017 DM (–) n = 2,363 | Significance Probability |
|-------------------|---------------------|-----------------------|--------------------------|
| Workload (quantity) | 3.4 (1.0)           | 3.4 (1.0)             | 0.559                    |
| Workload (quality)  | 3.1 (0.9)           | 3.1 (0.9)             | 0.481                    |
| Physical burden    | 3.0 (0.9)           | 3.0 (0.9)             | 0.672                    |
| Interpersonal stress | 3.1 (0.9)          | 3.2 (0.9)             | 0.056                    |
| Workplace stress   | 2.8 (0.9)           | 2.8 (0.9)             | 0.251                    |
| Degree of control  | 2.8 (1.0)           | 2.9 (1.0)             | 0.395                    |
| Skill utilization  | 2.8 (0.7)           | 2.9 (0.7)             | 0.017                    |
| Job fitness        | 2.7 (1.0)           | 2.8 (1.0)             | 0.094                    |
| Sense of reward    | 2.9 (1.0)           | 2.9 (1.0)             | 0.853                    |
| Stress response    |                     |                       |                          |
| Vigor              | 3.0 (1.0)           | 3.0 (1.0)             | 0.935                    |
| Irritation         | 3.3 (1.0)           | 3.4 (1.0)             | 0.177                    |
| Fatigue            | 3.1 (1.0)           | 3.2 (1.0)             | 0.428                    |
| Anxiety            | 3.3 (1.1)           | 3.4 (1.0)             | 0.514                    |
| Depression         | 3.5 (1.1)           | 3.6 (1.1)             | 0.587                    |
| Physical complaints| 3.3 (0.9)           | 3.4 (0.9)             | 0.686                    |

**Modifiers**

| Support, supervisor | 2.9 (1.1) | 2.9 (1.1) | 0.994 |
|---------------------|-----------|-----------|-------|
| Support, colleagues | 2.8 (1.0) | 2.8 (0.9) | 0.927 |
| Support, family and friends | 3.3 (1.3) | 3.4 (1.3) | 0.261 |

**Job and life satisfaction**

| 2017 DM (+) n = 241 | 2017 DM (–) n = 2,363 | Significance Probability |
|---------------------|-----------------------|--------------------------|
| Stress response     |                       |                          |
| Vigor              | 3.0 (1.0)             | 3.0 (1.0)               | 0.935                    |
| Irritation         | 3.3 (1.0)             | 3.4 (1.0)               | 0.177                    |
| Fatigue            | 3.1 (1.0)             | 3.2 (1.0)               | 0.428                    |
| Anxiety            | 3.3 (1.1)             | 3.4 (1.0)               | 0.514                    |
| Depression         | 3.5 (1.1)             | 3.6 (1.1)               | 0.587                    |
| Physical complaints| 3.3 (0.9)             | 3.4 (0.9)               | 0.686                    |

### Table 3. Number of participants with effective BJSQ data in 2013

| Job stressors     | 2017 DM (+) n = 241 | 2017 DM (–) n = 2,363 | Significance Probability |
|-------------------|---------------------|-----------------------|--------------------------|
| Workload (quantity) | 220 (91.3%)         | 2150 (91.0%)          |                          |
| Workload (quality)  | 220 (91.3%)         | 2144 (90.7%)          |                          |
| Physical burden    | 220 (91.3%)         | 2150 (91.0%)          |                          |
| Interpersonal stress | 220 (91.3%)      | 2146 (90.8%)          |                          |
| Workplace stress   | 220 (91.3%)         | 2149 (90.9%)          |                          |
| Degree of control  | 220 (91.3%)         | 2149 (90.9%)          |                          |
| Skill utilization  | 220 (91.3%)         | 2151 (91.0%)          |                          |
| Job fitness        | 220 (91.3%)         | 2151 (91.0%)          |                          |
| Sense of reward    | 220 (91.3%)         | 2151 (91.0%)          |                          |

### Table 4. Binomial logistic regression analysis (generalized linear model): odds ratios and 95% confidence intervals for BJSQ factors in 2013 (interpersonal stress, skill utilization, job fitness and irritation) in association with diabetes mellitus in 2017

| Stressors        | Significance Probability | Adjusted OR \( A \) | 95% Confidence Interval |
|------------------|--------------------------|---------------------|------------------------|
| Interpersonal    | 0.093                    | 1.334               | 0.953 – 1.868          |
| Skill utilization| 0.026                    | 1.632               | 1.061 – 2.510          |
| Job fitness      | 0.925                    | 1.014               | 0.754 – 1.365          |
| Irritation       | 0.130                    | 1.268               | 0.932 – 1.726          |

OR: odds ratio. Adjusted: age, HbA1c, antihyperlipidemic use, number of cigarettes smoked, drinking status, sleep time, night work status, and occupation. BJSQ: The Brief Job Stress Questionnaire.
Discussion

The results of our study suggest that, among the job stressors experienced in the workplace, "low skill utilization" is a risk factor for the development of DM. The stress levels associated with "low skill utilization" in 2013 were significantly higher in the 2017 DM group than in the non-DM group. How can skill utilization alter blood glucose control? The Labour, Health, and Welfare Organization investigated the interaction among extended working hours, body bio-regulatory system, and vascular endothelial function and whether these relationships could be affected by qualitative job stress factors (skill utilization and job control). The study examined the harmful health effects of working for long hours, for ≥1 and ≥6 months, using cardiovascular function, endocrine function, oxidative stress, and endothelial function indices as outcomes. The results showed that excessive cortisol secretion in individuals whose monthly overtime exceeded 45 hours was coupled with qualitative job stress "low skill utilization." Furthermore, to examine the harmful health effects of working for extended hours over a long period of time, scores on skill utilization were compared between two groups: those with cumulative overtime working hours of ≤250 or >250 hours during a 6-month period (from August 2010 to January 2011). The results showed that people with overtime work of >250 hours and who scored low on skill utilization had significantly higher levels of blood cortisol and urinary 8-isoprostane, a marker of oxidative stress, and tended to have higher urinary albumin concentrations than those scoring high on skill utilization. There was also a significantly positive correlation between blood cortisol and urinary 8-isoprostane levels in the overtime work >250 hours group. Based on these results, it was concluded that overtime work for more than 6 months at a workplace that provides little chance for the utilization of one’s skills may induce a prolonged stress response, which could ultimately lead to increased oxidative stress, possibly inducing endothelial dysfunction [10].

Based on previously reported findings that blood cortisol and urinary 8-isoprostane levels can increase significantly in response to the qualitative job stressor "low skill utilization," it is possible that excessive cortisol secretion or increased oxidative stress may result in a persistent state of hyperglycemia. In our study, there was no significant difference between the subjects who developed DM in 2017 and the subjects in the non-DM group with regard to estimated monthly overtime work. We think that differences in the survey methods of estimated monthly overtime work (based on self-reporting or based on pay stubs) could have affected this result, but the findings that blood cortisol and urinary 8-isoprostane levels can increase significantly in response to the qualitative job stressor "low skill utilization" are useful as a mechanism of hyperglycemia.

Several studies have investigated the relationship between mental stress and lifestyle-related diseases. One cross-sectional study conducted at Tohoku Rosai Hospital examined the association between quantitative and qualitative job stresses and lifestyle-related diseases and depressive tendencies in 1,075 people (751 ordinary citizens and 324 local government officials) who had undergone specific health checkups in 2010 and answered "I am currently employed." Qualitative job stress was investigated using the National Institute for Occupational Safety and Health (NIOSH) Generic Job Stress Questionnaire [11], proposed in the United States. Multiple logistic regression analysis was performed using the following objective variables: presence or absence of obesity, hypertension, DM, dyslipidemia, and depressive tendency. The results showed that the risk of "hypertension" and "depression" was 1.61 and 2.36 times higher, respectively, in the group with "low skill utilization" than in the group with "high skill utilization [12]." There was no relationship between skill utilization and DM in that study, and no relationship between skill utilization and blood pressure in our study. We think that differences in the study designs (cross-sectional or longitudinal), target area (Northeast Japan or Eastern and Central Japan), and eating habits (e.g. salt intake) could have affected these results. Moreover, important confounding factors such as antihypertensive drug use and salt intake status were not evaluated; it is possible that those results could have differed from those of previous studies.

In another study, the Japan Labour Health and Wel-
Job Stressors and Diabetes Development

fere Organization conducted a 5-year observational/longitudinal study from 2002 to 2006 of 3,219 employees aged 40 years or older (1,323 men and 1,896 women) working at 27 Rosai hospitals (which are associated with the Japan Labour, Health, and Safety Organization) nationwide to examine the association between the onset of brain and heart diseases and quantitative and qualitative workloads. Qualitative job stress was assessed by the NIOSH Generic Job Stress Questionnaire. The results showed that the risk of developing "brain or heart diseases" was 1.65 times higher in subjects with "low skill utilization" than in individuals with "high skill utilization", and the risk of development of "brain or heart diseases" was 1.66 times higher in the group with "low job control" than in the group with "high job control [13]."

The Japan Labour, Health, and Welfare Organization also conducted a cross-sectional study on the association between workload and the progression of atherosclerotic carotid lesions in 460 employees aged 40 years and older (195 men and 265 women) working at six Rosai hospitals between 2006 and 2007. The subjects completed various workload-related questionnaires and underwent carotid artery echography at the same time. Qualitative job stress was investigated by the NIOSH Generic Job Stress Questionnaire. The results showed that women scoring higher on "low skill utilization" had significantly higher "carotid plaque count" and larger "intima media thickness [13]." As described above, the qualitative job stressor "skill utilization" seems to be significantly associated with the onset of "hypertension" and "brain or heart diseases," as well as the progression of "atherosclerotic carotid lesions," and could be an important factor contributing to the onset of lifestyle-related diseases.

Mental health measures in the workplace have become a critical issue in recent years. Enforcement of Japan's revised Industrial Safety and Health Act in 2015 has made it mandatory for employers to implement stress checks. The stress check program is not limited to detecting and responding to workers with poor mental health at an early stage but also provides guidance for analyzing the stress check results at the workplace level so that the data can be utilized to improve the work environment [14]. Improving a workplace's environment includes measures to "prevent workers from developing poor health in the first place" and to "promote good health across the entire workplace." Mental health measures that focus on the positive psychological aspects of working have also been found to be useful in health promotion. One such example is "work engagement," which indicates that one takes pride in one's work and gains a sense of reward from one's work [15].

In the present study, "skill utilization" was found to be significantly associated with the presence or absence of DM after a 5-year follow-up. High utilization at work of one's knowledge, skills, and qualifications leads to "work engagement," which generates a favorable cycle through interactions.

There are several limitations to this study. First, the survey was conducted in workers of a single firm, and the actual conditions in other companies were not considered. It is necessary to collaborate with occupational health physicians of other companies in future studies to verify the correlations between job stressors and the onset of DM.

Furthermore, the onset of DM was defined only by HbA1c levels and the use of antidiabetic drugs. As detailed examinations, including a 75-g glucose tolerance test, were not conducted, one cannot rule out the occurrence of diabetes in some patients in the non-DM group.

Another limitation is that exercise status was defined only by existence; the analysis did not consider its amount or intensity. Also, there was no significant difference between those who developed DM in 2017 and those in the non-DM group with regard to the night shift ratio this time, and this requires detailed examination. The estimated monthly overtime work was based on self-reporting, and the accuracy was limited.

There were no associations between the amount of change in each factor, including "skill utilization", and the onset of DM from 2013 to 2017. As DM develops through the IGT state, it is important to evaluate the environmental factors several years before the onset of DM. This study was not evaluated before 2013, and longitudinal studies are limited.

The BJSQ is an indicator that varies among situations; thus, multiple evaluations are desirable and will be performed in the future.
Conclusions

Our study longitudinally examined the correlation between job stressors using the BJSQ and the development of DM in the employees of one company. Measures that promote mental health in the workplace are likely to generate a favorable cycle for DM control. It is essential to continue promoting comprehensive and advanced health management, not just to comply with the laws and regulations but also for fulfillment of the primary role of occupational health physicians.

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MS collected the data and wrote the manuscript. KE analyzed the data. YO and KT designed the study and reviewed the manuscript. YT reviewed the manuscript.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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Supplementary Material 1. Medical questionnaire

If applicable, please mark as □╱.

| Condition                                 | Under treatment | End of treatment | Treatment interrupted | Parents | Siblings |
|-------------------------------------------|-----------------|------------------|-----------------------|---------|----------|
| Hypertension                              | □               | □                | □                     | □       | □        |
| Cerebral hemorrhage/infarction            | □               | □                | □                     | □       | □        |
| Angina/myocardial infarction              | □               | □                | □                     | □       | □        |
| Arrhythmia                                | □               | □                | □                     | □       | □        |
| Hyperlipidemia                            | □               | □                | □                     | □       | □        |
| Diabetes                                  | □               | □                | □                     | □       | □        |
| Thyroid disease                           | □               | □                | □                     | □       | □        |
| Hyperuricemia (gout)                      | □               | □                | □                     | □       | □        |
| Blood diseases (such as anemia)           | □               | □                | □                     | □       | □        |
| Gastric/duodenal ulcer                    | □               | □                | □                     | □       | □        |
| Other gastrointestinal illnesses          | □               | □                | □                     | □       | □        |
| Liver disease                             | □               | □                | □                     | □       | □        |
| Gallstones and cholecystitis              | □               | □                | □                     | □       | □        |
| Caries                                    | □               | □                | □                     | □       | □        |
| Periodontitis/periodontal disease         | □               | □                | □                     | □       | □        |
| Bronchial asthma                          | □               | □                | □                     | □       | □        |
| Tuberculosis                              | □               | □                | □                     | □       | □        |
| Other lung diseases                       | □               | □                | □                     | □       | □        |

If taking any of the following medicines, please mark as □╱:

(1) Drugs that lower blood pressure
(2) Drugs that lower cholesterol and triglycerides
(3) Insulin or drugs that lower blood glucose level

Please answer the following questions about your work life.

(1) Occupation: Please answer only one main job.
   - Manager (office □/field □), Office staff (office □/field □), Station staff □, Conductor □, Driver □, Commander □, Rolling stock staff □, Track and structure staff □, Electrical engineering staff □, Medical staff □, Other □

(2) Do you work night shifts? Yes □ No □
   (If you are engaged in work from 22:00 to 5:00 the next day, please check “Yes.”)

(3) Overtime: Monthly ___ hours (or average daily ___ minutes)
   (If you do not work overtime, enter 0.)
Please answer the following questions about your daily life.

(1) Sleep: (1) Is your sleep regular? Yes □ No □
(2) Is your sleep good? Yes □ No □
(3) Average sleep time _ hours

(2) Do you smoke? Yes □ (Number of cigarettes _/day × _ years) (Including less than a month after quitting.)
No □ (I used to smoke □ and it has been _ years and _ months since I quit).

(3) Do you drink alcohol? Yes □ (Amount of consumed at one time _ go, __ times a week),
Sometimes □ (Amount of consumed at one time _ go, __ times a month),
No □ *1 go = 180 ml of sake = 20 g alcohol

(4) Do you have any hobbies? Yes □ No □

(5) Do you exercise regularly? Yes □ ((1) _ times/week (2) _ minutes/time) No □

Supplementary Material 2. The Brief Job Stress Questionnaire, English version

Please answer the following questions concerning your job by circling the number that best fits your situation.

| 1. I have an extremely large amount of work to do | Very much so | Moderately so | Somewhat | Not at all |
|-------------------------------------------------|-------------|--------------|----------|-----------|
| 2. I can’t complete my work in the required time |             |              |          |           |
| 3. I have to work as hard as I can              |             |              |          |           |
| 4. I have to pay very careful attention         |             |              |          |           |
| 5. My job is difficult in that it requires a high level of knowledge and technical skill |             |              |          |           |
| 6. I need to be constantly thinking about work throughout the working day |             |              |          |           |
| 7. My job requires a lot of physical work       |             |              |          |           |
| 8. I can work at my own pace                    |             |              |          |           |
| 9. I can choose how and in what order to do my work |             |              |          |           |
| 10. I can express my opinions on workplace policy |             |              |          |           |
| 11. My knowledge and skills are rarely used at work |             |              |          |           |
| 12. There are differences of opinion within my department |             |              |          |           |
| 13. My department does not get along well with other departments |             |              |          |           |
| 14. The atmosphere in my workplace is friendly  |             |              |          |           |
| 15. My working environment is poor (e.g. noise, lighting, temperature, ventilation) |             |              |          |           |
| 16. This job suits me well                      |             |              |          |           |
| 17. My job is worth doing                       |             |              |          |           |
Please answer the following questions concerning your health during the past month by circling the number that best fits your situation.

| Question                                                                 | Almost never | Sometimes | Often | Almost always |
|-------------------------------------------------------------------------|--------------|-----------|-------|---------------|
| 18. I have been very active                                              |              | 1 2 3 4   |       |               |
| 19. I have been full of energy                                           |              | 1 2 3 4   |       |               |
| 20. I have been lively                                                  |              | 1 2 3 4   |       |               |
| 21. I have felt angry                                                   |              | 1 2 3 4   |       |               |
| 22. I have been inwardly annoyed or aggravated                          |              | 1 2 3 4   |       |               |
| 23. I have felt irritable                                               |              | 1 2 3 4   |       |               |
| 24. I have felt extremely tired                                         |              | 1 2 3 4   |       |               |
| 25. I have felt exhausted                                               |              | 1 2 3 4   |       |               |
| 26. I have felt weary or listless                                        |              | 1 2 3 4   |       |               |
| 27. I have felt tense                                                   |              | 1 2 3 4   |       |               |
| 28. I have felt worried or insecure                                     |              | 1 2 3 4   |       |               |
| 29. I have felt restless                                                |              | 1 2 3 4   |       |               |
| 30. I have been depressed                                               |              | 1 2 3 4   |       |               |
| 31. I have thought that doing anything was a hassle                      |              | 1 2 3 4   |       |               |
| 32. I have been unable to concentrate                                   |              | 1 2 3 4   |       |               |
| 33. I have felt gloomy                                                  |              | 1 2 3 4   |       |               |
| 34. I have been unable to handle work                                    |              | 1 2 3 4   |       |               |
| 35. I have felt sad                                                     |              | 1 2 3 4   |       |               |
| 36. I have felt dizzy                                                   |              | 1 2 3 4   |       |               |
| 37. I have experienced joint pains                                      |              | 1 2 3 4   |       |               |
| 38. I have experienced headaches                                        |              | 1 2 3 4   |       |               |
| 39. I have had a stiff neck and / or shoulders                           |              | 1 2 3 4   |       |               |
| 40. I have had lower back pain                                          |              | 1 2 3 4   |       |               |
| 41. I have had eyestrain                                                |              | 1 2 3 4   |       |               |
| 42. I have experienced heart palpitations or shortness of breath        |              | 1 2 3 4   |       |               |
| 43. I have experienced stomach and/or intestine problems                |              | 1 2 3 4   |       |               |
| 44. I have lost my appetite                                             |              | 1 2 3 4   |       |               |
| 45. I have experienced diarrhea and/or constipation                     |              | 1 2 3 4   |       |               |
| 46. I haven't been able to sleep well                                   |              | 1 2 3 4   |       |               |
Please answer the following questions concerning people around you by circling the number that best fits your situation.

How freely can you talk with the following people?
47. Superiors ................................................................. 1 2 3 4
48. Co-workers ............................................................... 1 2 3 4
49. Spouse, family, friends, etc. ....................................... 1 2 3 4

How reliable are the following people when you are troubled?
50. Superiors ................................................................. 1 2 3 4
51. Co-workers ............................................................... 1 2 3 4
52. Spouse, family, friends, etc. ....................................... 1 2 3 4

How well will the following people listen to you when you ask for advice on personal matters?
53. Superiors ................................................................. 1 2 3 4
54. Co-workers ............................................................... 1 2 3 4
55. Spouse, family, friends, etc. ....................................... 1 2 3 4

Please answer the following questions concerning satisfaction by circling the number that best fits your situation.

56. I am satisfied with my job ............................................. 1 2 3 4
57. I am satisfied with my family life .................................. 1 2 3 4

Supplementary Material 3. Components of the Brief Job Stress Questionnaire

| Job Stressors     | Stress Response | Modifiers                                |
|-------------------|-----------------|------------------------------------------|
| Workload (quantity) | Vigor           | Support, supervisor                      |
| Workload (quality)  | Irritation      | Support, colleagues                     |
| Physical burden    | Fatigue         | Support, family and friends             |
| Interpersonal stress | Anxiety       | Job and life satisfaction               |
| Workplace stress   | Depression      | Physical complaints                     |
| Degree of control  |                 |                                          |
| Skill utilization  |                 |                                          |
| Job fitness        |                 |                                          |
| Sense of reward    |                 |                                          |

[9 subscales, 17 items] [6 subscales, 29 items] [4 subscales, 11 items]
Supplementary Material 4. STROBE Statement–Checklist of items that should be included in reports of cohort studies

| Item No | Recommendation                                                                                                                                                                                                 | Page No. |
|---------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|
| **Title and abstract** | 1. (a) Indicate the study’s design with a commonly used term in the title or the abstract.  
(b) Provide in the abstract an informative and balanced summary of what was done and what was found. | 3        |
| **Introduction** | 2. Explain the scientific background and rationale for the investigation being reported.                                                                                                                       | 4–5      |
| **Objectives** | 3. State specific objectives, including any prespecified hypotheses.                                                                                                                                             | 5        |
| **Methods** | 4. Present key elements of study design early in the paper.                                                                                                                                                     | 6–7      |
| **Setting** | 5. Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.                                                                               | 6–7      |
| **Participants** | 6. (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up.                                                                                   | 6–7      |
| **Variables** | 7. Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.                                                                         | 8–9      |
| **Data sources/measurement** | 8* For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group | 8–9      |
| **Bias** | 9. Describe any efforts to address potential sources of bias.                                                                                                                                                   | 8–9      |
| **Study size** | 10. Explain how the study size was arrived at.                                                                                                                                                                  | 6–7      |
| **Quantitative variables** | 11. Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why.                                                                              | 7        |
| **Statistical methods** | 12. (a) Describe all statistical methods, including those used to control for confounding.                                                                                                                     | 7        |
| **Results** | 13* (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed. | 6        |
| **Participants** | (b) Give reasons for non-participation at each stage.                                                                                                                                                         | 6        |
| **Descriptive data** | (c) Consider use of a flow diagram.                                                                                                                                                                             | 6        |
| 14* | (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders.                                                                       | 8–9      |
| **Outcome data** | (b) Indicate number of participants with missing data for each variable of interest.                                                                                                                          | 8        |
| **Main results** | (c) Summarise follow-up time (eg, average and total amount).                                                                                                                                                   | 8–9      |
| **Main results** | 15* Report numbers of outcome events or summary measures over time.                                                                                                                                             | 8–9      |
| **Main results** | 16. (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included. | 8–9      |
| **Main results** | (b) Report category boundaries when continuous variables were categorized.                                                                                                                                      | 9        |
| **Main results** | (c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period.                                                                                               | 9        |
## Supplementary Material 4 (Continued)

| Item No | Recommendation | Page No. |
|---------|----------------|----------|
| Other analyses 17 | Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses | 8–9 |

### Discussion

| Item No | Recommendation | Page No. |
|---------|----------------|----------|
| Key results 18 | Summarise key results with reference to study objectives | 9–10 |
| Limitations 19 | Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias | 13 |
| Interpretation 20 | Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence | 10–13 |
| Generalisability 21 | Discuss the generalisability (external validity) of the study results | 10–13 |

### Other information

| Item No | Recommendation | Page No. |
|---------|----------------|----------|
| Funding 22 | Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based | 15 |

*Give information separately for exposed and unexposed groups.

**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.

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