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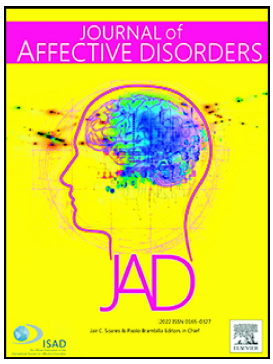

Effects of workplace measures against COVID-19 and employees' worry about them on the onset of major depressive episodes: A 13-month prospective study of full-time employees

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Running title: Workplace measures against COVID-19 and MDE

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Abstract

Background: Workplace measures against COVID-19 may prevent the onset of major depressive episode (MDE) in the working population. This 13-month prospective study aimed to investigate the association of the number of workplace measures against COVID-19 and employees' worry about the measures on the onset of MDE during COVID-19 outbreaks in Japan.

Methods: Data were collected from employees by using online questionnaires at baseline (May 2020) and the 7th survey (June 2021). The onset of MDE during the follow-up was retrospectively measured at the 7th survey, with a self-report scale based on the Mini-International Neuropsychiatric Interview according to the DSM-IV/DSM-5 criteria. Participants were asked to report the number of workplace measures against COVID-19 in their companies/organizations and their worry about these measures (scored 0-3). Multiple logistic regression was conducted of MDE on the number of workplace measures and worry about these, adjusting for demographic and work-related covariates and psychological distress at baseline.

Results: Among 968 respondents employed in May 2020, 827 completed the 7th survey in June 2021 (80%). We excluded 75 respondents who reported they had an MDE in May 2020 or earlier. Worry about workplace measures was significantly associated with the onset of MDE after adjusting for the covariates (OR for 1 score increase, 1.53; 95%CI, 1.02-2.32; p=0.042). No significant association was found between the number of workplace measures and the onset of MDE.

Conclusions: Worrying about workplace measures taken by company/organization may be a risk factor for the onset of an MDE among employees during the COVID-19 pandemic.

Keywords: Non-pharmaceutical interventions on COVID-19, mental disorders, working population, follow-up study, Japan

TITLE: Effects of workplace measures against COVID-19 and employees' worry about them on the onset of major depressive episodes: A 13-month prospective study of full-time employees

Running title: Workplace measures against COVID-19 and MDE

INTRODUCTION

Deteriorated mental health status in the community and working populations has been recognized as a major public health concern during the global pandemic of the novel coronavirus disease (COVID-19) since late 2019 (Giorgi et al. 2020; Abbott 2021). Studies during the epidemic have consistently reported a higher prevalence of psychiatric symptoms, such as depression, anxiety, post-traumatic stress symptoms, and insomnia (Cenat et al. 2021; Vizheh et al. 2020; Wu et al. 2021; Xiong et al. 2020) in these populations during the COVID-19 epidemic, and found that these symptoms actually increased along with the COVID-19 epidemic compared to the pre-epidemic era (Bierman and Schieman 2020; Kwong et al. 2020; Niedzwiedz et al. 2021; Pierce et al. 2020), although the impact may vary among subgroups such as people with less education and health care workers (Sasaki, Kuroda, et al. 2021; Sasaki et al. 2020a). Diagnosed common mental disorders such as major depressive episode (MDE) may also increase under such stressful conditions. However, no previous study has examined the onset of MDE and associated factors in the COVID-19 epidemic.

A review conducted in an early phase of the COVID-19 pandemic suggested that taking workplace measures to prevent and control COVID-19 mitigates poor mental health caused by the COVID-19 epidemic among workers (Giorgi et al. 2020). The International Labour Office (ILO) stated in its consensus-based guideline that information dissemination and communication about measures against COVID-19 in the workplace could be useful for preserving the mental health of workers (ILO 2020). Limited evidence suggested that both personal preventive practices such as

hand hygiene and wearing face masks, and organizational measures such as improvement of workplace hygiene and expressions of concern from the company were associated with less severe psychiatric symptoms in employees who returned to work after a COVID-19 outbreak (Tan et al. 2020). We have also found that the number of workplace measures against COVID-19 significantly and negatively correlated with psychological distress in a cross-sectional study of full-time employees in Japan in an early phase of COVID-19 epidemic (Sasaki et al. 2020b). Workplace measures against COVID-19 may prevent not only psychiatric symptoms, but also the onset of MDEs during the epidemic. However, workers may still worry about insufficiency or ineffectiveness of preventive measures taken against COVID-19 by their companies/organizations, depending on the employees' perceived needs and the characteristics of companies/organizations, such as type of industry, location, structures, and work content (ILO 2020). Employees' perceptions on effectiveness of implemented workplace preventive measures may be another good indicator of the quality of those preventive efforts. Workers' worry about workplace measures may also be associated with the onset of an MDE in the COVID-19 epidemic. To date, no study has been conducted on the impact of workplace measures against COVID-19 and employees' worry about these on the onset of MDEs in the working population.

This 13-month prospective study aimed to investigate the effect of workplace measures against COVID-19 and worry about the workplace measures taken, both reported by employees, on the onset of MDEs diagnosed according to DSM-IV/DSM-5, during repeated outbreaks of COVID-19 in Japan. We adjusted for global fear of COVID-19 and baseline health status, such as chronic conditions and psychological distress, as well as basic demographic and work-related characteristics as covariates.

METHODS

Study design and participants

This study was a 13-month prospective study from May 2020 until June 2021, embedded in a repeated panel survey of full-time workers of Japan during the COVID-19 epidemic, the E-COCO-J study (Sasaki et al. 2020a, 2020b; Sasaki, Imamura, et al. 2021; Sasaki, Kuroda, et al. 2021; Hidaka et al. 2021). A total of 1,448 full-time employees were recruited for the 1st survey in March 2020, during the initial, small COVID-19 epidemic in Japan, from participants of another larger survey conducted in 2019 by an Internet survey company from a large pool of preregistered community-dwelling residents across Japan. After the recruitment, seven (1st to 7th) consecutive surveys were conducted of the respondents between March 2020 and June 2021. We used the 2nd wave survey that was conducted in May 2020 to collect baseline data. This was because workplace measures against COVID-19 substantially changed between the 1st and 2nd wave surveys (Sasaki, Imamura, et al. 2021) and we could obtain data of stable measurement of the workplace measures by using the 2nd wave survey. We limited the subjects to those currently employed, excluding those who were unemployed, temporarily laid-off, on maternity-, childcare- or nursing care-leave, or on a long-term sick leave. The 7th survey used a self-rated version of M.I.N.I to ask participants' experience of major depressive episode (MDE) according to DSM-5 during the previous 12 months, as well as the month and year of the onset of the MDE if they experienced it. Based on the information collected, we excluded those who reported having had an MDE in May 2020 or earlier.

Measures

Major depressive episode (MDE)

The experience of an MDE was measured with a self-report scale developed based on the Mini-International Neuropsychiatric Interview (M.I.N.I.) (Sheehan et al. 1998; Otsubo et al.

2005) according to the DSM-IV/DSM-5 criteria (American 2013). Nine questions from the MDE section of the M.I.N.I. were used to assess whether a participant had had an MDE in the past. The participant was asked to recall any depressive episode in the previous 1.5 years since January 2020, i.e., the beginning of the COVID-19 epidemic in Japan. If a participant had enough symptoms for an MDE, an additional question asked the onset month and year when the participant first had symptoms of an MDE. We calculated months (1-13 months) from the baseline (May 2020) to the MDE. We excluded a participant if he/she reported having had the first MDE in May 2020 or earlier. The sensitivity and specificity of this instrument for the clinical diagnosis of major depression were reported in a pilot study as 0.86 and 0.67, respectively, in a sample of psychiatric outpatients (n=31).

Workplace measures against COVID-19

The degree of implementation of workplace measures for prevention against and control of COVID-19 was assessed by using a 23-item original scale, which was developed based on workplace measures in a past outbreak of novel influenza and a discussion by occupational health professionals (Sasaki, Imamura et al. 2021; Sasaki et al. 2020b). Briefly, the items covered the following areas: (a) individual-based preventive measures (masks, etc.); (b) measures to reduce the risk of infection in the workplace; (c) procedure for staying at home and clinical contact; (d) temporary leave when infected; (e) accommodation of high-risk people (e.g., with chronic conditions); (f) reliable information resources; and (g) the duration of special measures. Responses to each item were dichotomized into “implemented” or “not implemented”. We calculated the number of implemented measures as an indicator of the degree of implementation of workplace measures, which ranged from 0 to 23. The internal consistency reliability was 0.897 at the 2nd survey. The indicator was stable, with high concordance between the 2nd and 3rd

surveys (intraclass correlation coefficient [ICC], 0.748). The score 0-23 was used as a continuous variable in the main analysis; a categorization of the score into the tertiles (low, moderate, and high implementation) was made for supplemental analyses. The same scale was used in the 3rd, 4th, 5th, and 6th surveys.

Worry about workplace measures

A single item question asked if a respondent worried about the insufficiency of workplace measures taken by his/her company/organization. The 4-point responses (strongly agree, somewhat agree, somewhat disagree, and strongly disagree) were scored 3, 2, 1, and 0, respectively. The concordance between the 2nd and 3rd surveys was 0.505 in intraclass correlation coefficient (ICC). The same scale was asked in the 3rd, 4th, 5th, and 6th surveys. The score was used as a continuous variable in the main analysis, while the four categories were used for supplementary analyses. The worry (or a concern) is theoretically defined as a psychological threat (a stressor) rather than a stress response, such as anxiety.

Covariates

All covariates were measured at baseline (the 2nd survey). The demographic covariates included sex (male or female), age (20-34 years, 35-49 years, or 50+ years), marital status (single or married), and living in areas with the governmental emergency call in May 2020 (yes or no). Job-related covariates included occupation (managers, non-manual workers, manual workers, or health care workers), remote work (no or any type of remote work). Health-related covariates included chronic physical condition (any of 10 predetermined physical conditions) and psychological distress (depression and anxiety) in the last 30 days, measured by using the Kessler 6 (K6) scale (Kessler et al. 2003; Furukawa et al. 2008), and used as a continuous score (0-24).

Fear of COVID-19 was measured using a single item scale, "Do you worry about COVID-19?"; the 6-point Likert-type response was scored from 0 to 5 (Hidaka et al. 2021).

Statistical analysis

The numbers and proportions of participants were tabulated by groups, classified based on the baseline covariates. The averages of the number of workplace measures and the score of worry about workplace measures were compared between the onset cases of MDE and the other respondents (t-test). Multiple logistic regression was conducted for the onset of MDEs on the number of workplace measures against COVID-19 and the score of worry about workplace measures, adjusting for the other covariates (sex, age groups, marital status, occupation, remote work, living in emergency call areas, fear of COVID-19, chronic condition, and psychological distress).

As supplemental analyses, we used the Cox proportional hazard model. This was because the Cox proportional hazard model is able to (1) use information from censored cases, (2) consider the timing of onset of MDE, and also (3) incorporate information of time-dependent change of exposure variables (i.e., the number of and worry about the measures). However, it should be noted that, in this study, the first merit may be small because the sample was limited to respondents who completed both baseline and last follow-ups surveys; the second merit may be offset by unviable reporting of the onset month of MDE by respondents. First, the Cox proportional hazard model was conducted for the onset of MDEs and the onset months since the baseline on the baseline variables of workplace measures against COVID-19 and worry about workplace measures, adjusting for the other covariates. Second, the Cox model was conducted for the onset of MDEs and the onset months since the baseline on the time-dependent variables of workplace measures against COVID-19 and worry about workplace measures, adjusting for the

other covariates at baseline. In the latter analysis, we used responses immediately before the onset of an MDE for these two variables (workplace measures against COVID-19 and worry about workplace measures). If the onset occurred in the same month of a survey, we used a response from the previous survey. If the response immediately before the onset was missing, we assigned a response from a previous survey. In another series of supplementary analyses, we conducted similar multiple logistic regression and Cox proportional hazard models using the categories of exposure variables: the tertiles of the number of workplace measures and the four categories of worry about workplace measures. Statistical significance was set as a two-sided $p<0.05$. SPSS 26.0 (IBM Corp., Armonk, NY, USA) Japanese version was used.

RESULTS

Participant flow

A total of 1,032 responded to the 2nd survey of May 2020 (**Figure 1**). We excluded those who were unemployed (n=17), temporarily laid-off (n=28), on maternity-, childcare- or nursing care-leave (n=17), or on a long-term sick leave (n=2). Among 968 respondents currently employed in May 2020, 827 participated in the 7th survey in June 2021 (80.1%). Most respondents participated in the other follow-up surveys in-between: 882 (91.1%) for the 3rd survey; 860 (88.8%) for the 4th survey; 857 (88.5%) for the 5th survey; 843 (87.1%) for the 6th survey. In the final step, we excluded 75 who reported they had experienced MDE in May 2020 or earlier. Data from the remaining 752 participants were used for the analyses.

Participant baseline characteristics

The respondents were distributed equally in terms of sex, age group, marital status (**Table 1**). About half had non-manual jobs; about 10% were HCWs. One third engaged in remote work.

Most lived in the COVID-19-related state of emergency areas as of May 2021 and felt fear about COVID-19. Thirteen percent had chronic conditions. The number (proportion, %) of respondents by the response to worry about workplace measures against COVID-19 taken by their companies/organizations were: 96 (12.8%) for strongly agree; 284 (38%) for somewhat agree; 310 (41.2%) for somewhat disagree; and 62 (8.2%) for strongly disagree. The number of workplace measures and the score of worry about workplace measures significantly and negatively correlated each other (Pearson's r= -0.134, p<0.001).

Incidence of MDE

Among the final 752 participants who were free from MDEs at or before baseline, 52 (6.9%) were diagnosed with an MDE during the 13-month follow-up between June 2020 and June 2021. The incidence was calculated as 0.066 per year over 9,422 person-months. The mean number (standard deviation, SD) of workplace measures was 14.6 (5.7) for non-MDE cases (N=700) and 12.9 (5.8) for MDE cases (N=52), with no significant difference (t-test, p=0.397). The mean score of worry about the measures was 1.5 (0.8) for non-MDE cases and 1.9 (0.9) for MDE cases, with a significant difference (t-test, p=0.001).

Association of the number of and worry about workplace measures with MDE

Worry about workplace measures was significantly associated with the onset of an MDE after adjusting for the covariates in the multiple logistic regression (OR for 1 score change, 1.53; 95%CI, 1.02-2.32, p=0.042) (**Table 2**). The number of workplace measures against COVID-19 was not significantly associated with the onset of an MDE, while the OR for 1 point change was smaller than 1 (OR, 0.99; 95%CI, 0.94-1.05; p=0.766). Marital status, living in emergency call area, and psychological distress were significantly associated with the onset of an MDE (p=0.006,

p=0,039, and p<0.001, respectively).

The supplemental analyses showed similar results. The Cox proportional hazard model with all variables measured at baseline (**Supplemental table 1**, **left**) showed that worry about workplace measures was not significantly, but qualitatively similarly to findings with the other model, associated with the onset of MDE after adjusting for the covariates (HR for 1 score change, 1.38; 95%CI, 0.95; p=0.092). The Cox model with time-dependent variables for workplace measures and worry about measures (**Supplemental table 1, right**) showed worry about workplace measures was not significantly, but similarly, associated with the onset of MDE (HR for 1 score change, 1.40; 95%CI, 0.96-2.02, p=0.078). The number of workplace measures was not associated with the onset of MDE in either of the Cox proportional hazard models (HR for 1 score change, 0.99; 95%CI, 0.94-1.04, p=0.732; HR for 1 score change, 0.99; 95%CI, 0.94-1.05, p=0.772, respectively).

Association of categories of the number of and worry about workplace measures with MDE

The numbers (proportions) of MDE cases by the tertiles of the number of workplace measures were: 19 (7.9%) for the lowest (0-12) group (N=241); 16 (6.7%) for the middle (13-17) group (N=240); and 17 (6.3%) for the highest (18-23) group (chi-square=0.5, DF=2, p=0.760). The numbers (proportions) of MDE cases by worry about workplace measures were: 16 (16.7%) for strongly agree (N=96); 19 (6.7%) for somewhat agree (N=284); 13 (4.2%) for somewhat disagree (N=310); and 4 (6.5%) for strongly disagree (N=62) (chi-square=17.8, DF=3, p<0.001).

In a multiple logistic regression adjusting the covariates (**Supplemental table 2**), the tertiles of the number of workplace measures were not significantly associated with MDE (Wald chi-square=0.1, DF=2; p=0.956): taking the lowest group as the reference, odds ratios (95%CI) were 1.12 (0.50 – 2.48) for the middle group; and 1.01 (0.45 – 2.29) for the highest group. The

categories of worry about the measures were significantly associated with MDE (Wald chi-square=9.0, DF=3; p=0.029): taking the strongly agree group as the reference, odds ratios (95%CI) were 0.39 (0.17 – 0.89) for the somewhat agree group; 0.26 (0.11 – 0.66) for the somewhat agree group; and 0.56 (0.15 – 2.15) for the strongly disagree group.

In a Cox proportional hazard model based on the baseline covariates (**Supplemental table 3, left**), the tertiles of the number of workplace measures were not significantly associated with MDE (Wald chi-square=0.1, DF=2; p=0.961): taking the lowest group as the reference, odds ratios (95%CI) were 1.11 (0.54 – 2.26) for the middle group; and 1.0 (0.50 – 2.19) for the highest group. The categories of worry about the measures as a whole were not significantly associated with MDE (Wald chi-square=6.2, DF=3; p=0.102): taking the strongly agree group as the reference, odds ratios (95%CI) were 0.52 (0.25 – 1.07) for the somewhat agree group; 0.37 (0.16 – 0.85) for the somewhat agree group; and 0.69 (0.20 – 2.32) for the strongly disagree group. Similarly, in a Cox proportional hazard model using time-dependent covariates (**Supplemental table 3, right**), the tertiles of the number of workplace measures were not significantly associated with MDE (Wald chi-square=0.0, DF=2; p=0.988): taking the lowest group as the reference, odds ratios (95%CI) were 1.06 (0.52 – 2.15) for the middle group; and 1.04 (0.50 – 2.16) for the highest group. The categories of worry about the measures as a whole were not significantly associated with MDE (Wald chi-square=6.2, DF=3; p=0.084): taking the strongly agree group as the reference, odds ratios (95%CI) were 0.51 (0.25 – 1.06) for the somewhat agree group; 0.36 (0.16 – 0.82) for the somewhat agree group; and 0.69 (0.20 – 2.34) for the strongly disagree group.

DISCUSSION

The present study found that worry about workplace measures was significantly associated with the onset of MDE during the 13-month follow-up, in the multiple logistic regression after

adjusting for the covariates (OR for 1 score increase, 1.53; 95%CI, 1.02-2.32; p=0.042). In the supplemental analyses, Findings of the supplemental analyses using Cox proportional hazard models were also in line with this: the association was not statistically significant, but qualitatively similar to findings with the multiple logistic regression model. The number of workplace measures implemented by companies/organizations of the respondents was not significantly associated with the onset of an MDE.

Worrying about workplace measures taken by company/organization was associated with the onset of an MDE in the multiple logistic regression after adjusting for the covariates including psychological distress and fear of COVID-19 at baseline. The estimated odds ratio for 1 score change was 1.5. The association was not significant in the supplemental analyses applying Cox proportional hazard models. This may be due to the lack of the statistical power and/or an unreliable reporting of the onset month of MDE by respondents. However, the magnitude of the associations (hazard ratios for 1 score change) was similar to one observed with the multiple logistic regression that showed statistical significance. Worrying about workplace measures against COVID-19 may be a risk factor of MDE among employees in the COVID-19 pandemic. Further research needs to replicate the finding. An additional multiple logistic regression also showed a significant association between the four categories of worry about workplace measures and MDE onset: compared to respondents who strongly agreed about their worry about workplace measures, respondents who somewhat agreed and somewhat disagreed had significantly lower risks (odds ratios, 0.39 and 0.26, respectively). Cox proportional hazard models yielded similar findings. Respondents in the last category who strongly disagreed also showed a non-significantly but lower risk of MDE than that of respondents who strongly agreed (odds ratio, 0.56), which was greater than that of respondents who somewhat agreed. The relationship between the degree of worry about workplace measures and MDE may be U-shaped. However, this may be by chance

due to the small number of respondents in the last category. Further studies are needed to confirm this non-linear association with a larger sample.

The findings suggest that respondents with strong worry about workplace measures are more likely to develop MDE. These respondents may keep working with this feeling in the COVID-19 pandemic, with little say to change the top-down policy of workplace measures. The situation may provoke learned helplessness of the participants, which is known as a risk factor for an MDE (Maier & Seligman, 2016). The finding is also in line with studies showing that job satisfaction has been associated with depression (Faragher et al, 2005). Worry about workplace measures may reflect lack of satisfaction on a specific aspect of work, i.e. workplace measures against COVID-19, which may lead to the onset of MDE. However, it is possible that some respondents may express excessive worry about workplace measures because of other reasons. For instance, neurotic traits that may exist behind worrying about workplace measures could increase the risk of MDE, although we tried to minimize this bias by adjusting for fear of COVID-19 and psychological distress. Respondents expressing strong worry about workplace measures may also be dissatisfied with other aspects of their work, such as the interpersonal relationship at work or salary, which may increase the risk of an MDE. Lack of communication at work may underlie worry about workplace measures, which has been associated with poor mental health of workers in the COVID-19 pandemic (Giorgi et al., 2020). Further careful research is needed to conclude the causal association between worry about workplace measures against COVID-19 and MDE.

The number of workplace measures against COVID-19 was not significantly associated with the onset of an MDE and odds ratio was very small. This contradicts our previous cross-sectional finding of the association between the number of workplace measures and psychological distress in the same sample (Sasaki et al. 2020b). Since the reported effect was small (Sasaki et al. 2020b), it may not exist for a longer-term period. The effect of workplace measures on better mental

health may not apply to an MDE, a more severe form of psychopathology. The number of workplace measures may be too simple to be a good judge of sufficiency or effectiveness for prevention of COVID-19. Some workplace measures, such as forced social distancing, may rather increase stress among employees (Hamouche, 2020). Some of the measures may not be relevant to some industries or workplace structures; the quality, not the number of workplace measures may be more important. It would be interesting to investigate if any specific item of the scale is associated with the onset of an MDE. Further research is also required using a scale of quantity and quality of workplace measures against COVID-19.

The present study implies that focusing on worry about workplace measures may be more important for preventing MDE than just increasing the number of workplace measures, while there was a weak negative association between these two. Implementing workplace measures against COVID-19 meeting employees' concerns and needs may be essential. Communication between an employer and employees is recommended to reduce employees' worry about workplace measures (ILO 2020). Providing information and rationale for implemented (or unimplemented) workplace measures, and encouraging worker participation in its planning, such as listening to the voices of employees, may reduce employee worry about workplace measures and then the risk of MDE. A group of employees with strong worry about workplace measures may be the priority target of such communication. An intervention study is warranted using such an approach to prevent MDEs of workers in future.

Limitations

The sample of the study may not represent the whole working population in Japan, being biased to those who frequently use the Internet, such as non-manual workers. The 13-month follow-up rate was relatively high (84%). However, the attrition may have caused a selection bias. For instance,

the association between workplace measures or worry about these and MDEs may be underestimated if more participants with an MDE and poorly implemented workplace measures died because of COVID-19 infection; although this is not very likely considering the low mortality rate due to COVID-19 in Japan. Participants who were dissatisfied with workplace measures may have reported MDEs more frequently to indicate their frustration. Factors associated with both negative reporting of workplace measures and worry about these and self-reported MDEs, such as a neurotic personality or high perception of COVID-19 infection risk, may confound the findings, although we adjusted for global fear of COVID-19 and psychological distress at baseline to minimize such bias. The scale of worry about workplace measures showed only moderate stability between the surveys, which may lead to the underestimation of the association with MDE. The number of workplace measures was self-reported, and may be unreliable because employees may not be fully informed of the measures or able to exactly recall measures taken. Since the scale was developed in Japan, it may not be applicable to other countries that have a different system for occupational health and safety. Workplace responses to the COVID-19 pandemic varied among industrial sectors and occupations (Sasaki, Imamura et al., 2021); Risks of COVID-19 infection (Yoshikawa & Kawachi, 2021) and fear of COVID-19 and psychological distress (Midorikawa et al., 2021) also varied among industrial sectors. While we adjusted for major occupational categories including health care workers, industry and occupation may confound the findings. Moreover, it is not clear if the observed association may be different among types of industry or occupation. Type of employment contract, such as permanent or fixed-term, may also confound the finding, and may moderate the association. Some important covariates may not be adequately adjusted in the study. For instance, we did not ask a question to identify respondents being separated/divorced that are at a greater risk of MDE. We did not adjust for changes of covariates at the follow-up surveys. Manual workers were more

represented in the study sample compared to the whole employed population of Japan (23% vs 15%, respectively), while sex and age distribution of the sample was close to it (Sasaki et al., 2020a). The findings may more reflect the situations in this occupation. The self-report M.I.N.I. was not fully validated to measure an MDE. The measurement errors may result in the underestimation of the association with the onset of an MDE. The sample size was small, with only 52 cases developing MDE. The study may not be statistically powerful enough, which may lead to a non-significant association between worry about workplace measures and MDE onset in supplementary Cox proportional hazard analyses. The present findings should be replicated with a larger sample with established measures of worry about workplace measures and MDE onset, considering occupational differences and adjusting for possible confounders.

Conclusions

The present study found that employees' worry about workplace measures against COVID-19 was associated with an onset of an MDE during the 13-month follow-up. Employees' worry about the workplace measures may be an emerging risk factor for MDE in the COVID-19 epidemic.

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Figure 1. Participant flow chart of a 13-month prospective study of full-time employees during the COVID-19 epidemic.

Table 1. Baseline characteristics of respondents who were free from major depressive episodes (MDE) at baseline (N=752)

	N	%	Mean	SD
Sex				
Male	396	52.7%		
Female	356	47.3%		
Age (years)				
20-34	206	27.4%		
35-49	307	40.8%		
50+	239	31.8%		
Marital status				
Single	356	47.3%		
Married	396	52.7%		
Occupation				
Manager	89	11.8%		
Non-manual	413	54.9%		
Manual	176	23.4%		
Health care	74	9.8%		
Remote work				
No	509	67.7%		
Yes	243	32.3%		
Emergency call area				
No	223	29.7%		
Yes	529	70.3%		
Chronic condition				
No	656	87.2%		
Yes	96	12.8%		
Fear for COVID-19 (score, 0-5)			3.5	1.1
Psychological distress (K6 score, 0-24)			4.5	4.8
The number of workplace measures against COVID-19 (0-23) *			14.6	5.7
Worry about workplace measures (score, 0-3) *			1.6	0.8

* The ranges of the score in the parentheses.

Table 2. Association of workplace measures against COVID-19 and worry about workplace measures with the onset of MDE during 13-month follow-up adjusting for covariates using multiple logistic regression: odd ratios (ORs) and 95% confidence intervals (CIs)

	OR	95% CI		p
Sex (female)	1.39	0.68	2.86	0.371
Age (years)				
20-34	1.00			
35-49	1.73	0.79	3.78	0.168
50+	2.03	0.83	5.19	0.118
Marital status (married)	0.35	0.17	0.75	0.006
Occupation				
Manager	1.00			
Non-manual	1.09	0.28	4.36	0.898
Manual	1.26	0.29	5.59	0.759
Health care	2.51	0.54	11.75	0.242
Remote work (yes)	1.81	0.82	4.03	0.145
Emergency call area (yes)	0.49	0.25	0.97	0.039
Fear for COVID-19 (0-5)*	1.15	0.85	1.55	0.368
Chronic condition (yes)	1.43	0.61	3.34	0.405
Psychological distress (K6 score, 0-24)*	1.19	1.12	1.26	<0.001
The number of workplace measures against COVID-19 (0-23)*	0.99	0.94	1.05	0.766
Worry about workplace measures (0-2)*	1.53	1.02	2.32	0.042

* The ranges of the score in the parentheses. For these variables, OR for 1 score increase and the 95%CIs were shown.

DISCLOSURE

Authors' Contributions: NK was in charge of this study, supervising the process and of providing his expert opinion. NK organized the study design. HA, NS and NK analyzed the data. Collaborators KI, RK and KT ensured that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved. NK wrote the first draft of the manuscript, and all other authors critically revised it. All authors approved the final version of the manuscript.

Approval of the research protocol: This study was approved by the Research Ethics Committee of the Graduate School of Medicine/Faculty of Medicine, The University of Tokyo, No. 10856-(2)(3)(4)(5).

Informed consent: Online informed consent was obtained from all participants with full disclosure and explanation of the purpose and procedures of this study. We explained that their participation was voluntary, and they can withdraw consent for any reason, simply by not completing the questionnaire.

Registry and registration number of the study/trial: N/A.

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Highlights

- It is unknown if workplace measures taken against COVID-19 by companies/organizations protect workers from having a major depressive episode (MDE) in the COVID-19 epidemic.
- The score of worry about workplace measures was significantly associated with the onset of MDE among full-time employees at a 13-month follow-up during repeated outbreaks of COVID-19 in Japan, after adjusting for the covariates.
- Addressing employees' worry about workplace measures taken by company/organization may mitigate the risk of MDEs during the COVID-19 epidemic.