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The Psychological Burden of Attention-Deficit/Hyperactivity Disorder Traits on Medical Workers Under the COVID-19 Outbreak: A Cross-Sectional Web-Based Questionnaire Survey

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ABSTRACT

Objectives:

There are numerous reports on the psychological burden of medical workers after the COVID-19 outbreak; however, no study has examined the influence of developmental characteristics on the mental health of medical workers. The objective of this study was to examine whether the developmental characteristics of medical workers are associated with anxiety and depression after the COVID-19 outbreak.

Design:

We conducted an online cross-sectional questionnaire survey in October 2020.

Participants and setting:

The data of 640 medical workers were analyzed. The questionnaire included items on sociodemographic data, changes in their life after the COVID-19 outbreak, and symptoms of depression, anxiety, attention deficit/hyperactivity disorder (ADHD) traits, and autism spectrum disorder traits.

Main outcomes:

Depression symptoms were assessed by the Patient Health Questionnaire-9 (PHQ-9) and anxiety symptoms were assessed by the Generalized Anxiety Disorder-7 (GAD-7). A series of hierarchical multiple regression analyses were performed to test the effects of developmental characteristics on depression and anxiety symptoms after controlling for sociodemographic factors and changes in participants' lives after the COVID-19 outbreak.

Results:

Increases in physical and psychological burden were observed in 49.1% and 78.3% of the subjects, respectively. The results of a multiple regression analysis showed that ADHD traits were significantly associated with both depression (β=0.390, $p<0.001$) and anxiety (β=0.426, $p<0.001$). Autistic traits were significantly associated with depression (β=0.069, $p<0.05$) but not anxiety. Increased physical and psychological burden, being female, medical workers other than physicians and nurses, fear of COVID-19,

and experience of discrimination were also significantly associated with both depression and anxiety.

Conclusion:

Globally, the burden on medical workers increased. This study suggested that medical workers with higher ADHD traits may need special attention during the COVID-19 pandemic.

ARTICLE SUMMARY

Strengths and Limitations of this study:

- First study to examine the association between developmental characteristics and psychological burden of medical workers under the COVID-19 outbreak.
- Sufficiently large sample size.
- Broad assessment on occupational environment and the changes in daily lifestyle under the COVID-19 outbreak.
- Despite an attempt to obtain a diverse sample of medical workers, the sample was skewed toward certain professions.
- Developmental characteristics in this study were not formal diagnoses.

INTRODUCTION

Previous studies have shown that outbreaks of serious infectious diseases can place a heavy psychological burden on health care workers.[1-4] Immediately after the coronavirus disease 2019 (COVID-19) outbreak, it was pointed out that mental health problems can emerge among medical workers due to the fear of risking infection to their own family, friends, and colleagues, with uncertainty about the future, and stigmatization of themselves.[5] There have already been a number of studies reporting mental health problems among health care workers working against COVID-19.[1-4 6-12] However, these reports were mainly from regions such as China, the United States, and European countries that experienced severe consequences of the COVID-19 pandemic.

Compared to the above-mentioned countries, the number of new cases and deaths caused by COVID-19 in Japan was small (Figure 1);[13] hence, people experiencing loss through death were considered rare. Although there has been no government-imposed lockdown with legal restraints, the further spread of COVID-19 has been prevented by only a request for self-restraint in social activities by the Prime Minister and prefectural governors.[14] People's compliance with the request of wearing masks and avoiding unnecessary outings might have contributed to preventing the spread of the disease, but their effectiveness are not clear. In contrast, medical institutes, along with restaurants/bars and music events, were reported to have contributed to cluster outbreaks,[15] leading to increased stigma and discrimination against health care workers. Thus, it is not only the fear of infection by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), but also the increased workload related to infection control, stigma/discrimination, and stress in health care workers. When health care workers experience physical or mental health problems, it could lead to a decline in health care services and ultimately affect patients.[16] As maintaining the quality of health care services affects the interests of society as a whole, reducing the physical and mental burden of health care providers would be the most essential factor to overcome the COVID-19 pandemic.

People with specific developmental characteristics may experience greater psychological burden during the COVID-19 pandemic.[17-22] However, there have been no reports on the psychological effects of the COVID-19 pandemic on adult health care workers with attention-deficit hyperactivity disorder (ADHD) and/or autistic traits. In recent years, ADHD and autistic traits have been regarded as spectra and

have been shown to co-occur.[23] ADHD traits may make compliance with the COVID-19 precautions highly stressful because of factors like inattention, hyperactivity, and impulsivity. Similarly, autism spectrum disorder (ASD) traits may make people vulnerable to anxiety because of the need to adjust their daily lifestyles to the COVID-19 crisis. Considering this, we hypothesized that medical workers with developmental characteristics such as ADHD and autistic traits experience depression and anxiety symptoms to a greater extent during the COVID-19 outbreak due to changes in their daily lifestyle. We investigated the constraints from the COVID-19 outbreak on daily lifestyles along with the physical and psychological burdens among medical workers. After controlling these variables, we aimed to determine the effect of ADHD and autistic traits on depression and anxiety symptoms among medical workers.

METHODS

Setting and study population

The present study was conducted as part of a comprehensive research project [MEdical Workers' MEntal health and Working conditions in Japan under the COVID-19 pandemic (MEW2-J-COVID) project] to investigate the mental health, work, lifestyle, and distraction of medical workers after the COVID-19 outbreak. This cross-sectional web-based questionnaire survey was conducted between October 1 and 30, 2020. Participants were recruited via snowball sampling and accessed the link to a Google Form containing the questionnaire posted on the National Center of Neurology and Psychiatry website. Informed consent was obtained from all participants via the survey website.

Of the 712 participants who completed the Google Form questionnaire, the data of 683 participants were analyzed. Data of 29 participants were excluded because they were duplicates (n=24), were under 20 years or not medical workers (n=3), contained garbled data (n=1), or contained invalid data on working hours (n=1). Of these, those not working at a medical institution (n=25) and working less than 15 days in a month (n=18) were excluded. Totally, 43 participants were excluded. Finally, 640 participants were included in the analyses.

Assessments

Questionnaires consisted of the sociodemographic questionnaire, the Patient Health Questionnaire-9

(PHQ-9) for estimating depressive symptoms,[24 25] the Generalized Anxiety Disorder-7 (GAD-7) for assessing anxiety symptoms,[26 27] the Adult ADHD Self-Report Scale (ASRS-V1.1) for estimating ADHD symptoms,[28 29] and the Autism Spectrum Quotient-10 (AQ-10) for quantifying autistic traits.[30 31]

Main outcome measures

Depression symptoms were assessed by the PHQ-9.[24 25] Based directly on the nine diagnostic criteria for major depressive disorder in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV),[32] the scale consists of nine items that assess the frequency with which nine depressive symptoms had occurred in the past 2 weeks. Participants rated items as 0, 1, 2, or 3 for "not at all," "several days," "more than half the days," and "nearly every day," respectively. Responses to each item were summed to provide a single score ranging from 0 to 27, with higher scores indicating more severe depressive symptoms.

Anxiety symptoms were assessed by the GAD-7.[26 27] The GAD-7 is derived from the 13-item criteria for GAD in the DSM-IV.[32] It consists of seven items with the highest correlation to the 13-item scale score. Participants rated the frequency of seven anxiety symptoms during the last 2 weeks as 0, 1, 2, or 3 for "not at all," "several days," "more than half the days," and "nearly every day," respectively. The responses to each item were summed to provide a single score ranging from 0 to 21, with higher scores indicating more severe anxiety symptoms.

Predictors—developmental characteristics

ADHD traits were assessed by the ASRS-V1.1 Screener.[28 29] The ASRS-V1.1 Screener was derived from the 18-item criteria for ADHD in the DSM-IV,[32] consisting of six questions considered most predictive of symptoms consistent with ADHD. The six-item questionnaire includes questions on inattention (four items) and hyperactivity symptoms (two items). Participants rated the frequency of ADHD symptoms over the past 6 months as 0, 1, 2, 3, or 4 for "never," "rarely," "sometimes," "often," and "very often," respectively. The responses to each item were summed to provide a single score ranging from 0 to 24, with higher scores indicating higher ADHD traits.

Autistic traits were assessed by the AQ-10.[30 31] The AQ-50, an original version of the AQ-10, was originally developed as a tool for screening autistic traits in intellectually able adults. Albeit a short version

of the AQ-50, the AQ-10 has been well validated for measuring autistic traits.[33] Responses are rated on a four-point scale: "definitely disagree," "slightly disagree," "slightly agree," and "definitely agree." Responses indicating autistic traits were scored 1, while other responses were scored 0 (for five items, "definitely disagree" and "slightly disagree" were scored 1, but for the five reverse-scored items, "slightly agree" and "definitely agree" were scored 1). The responses to each item were summed to provide a single score ranging from 0 to 10, with higher scores indicating a higher level of autistic traits.

Predictors—changes in lifestyle

With regard to changes in lifestyle after the COVID-19 outbreak, changes in physical and psychological burden were rated: "markedly decreased," "decreased," "unchanged," "increased," or "markedly increased." Also, changes in income, frequency of going out, and interpersonal interactions (including online interactions) were assessed using the rate of change: "Greater than or equal to 150%," "110 to 150%," "90 to 110 %," "50 to 90%," or "Less than 50%."

Other covariates

The questionnaire included items on demographic characteristics, such as age (stratified by decade), sex, body mass index (BMI), residential area (urban, suburban, or rural), number of households, smoking habit (yes/no), habitual alcohol consumption (yes/no), and history of COVID-19 infection (yes/no). Participants' work status including occupation, commuting time (< 30 min, 30 min to 1 h, or ≥ 1 h), working hours per day and number of workdays per month, engagement in night-shift (yes/no), frequency of contact with confirmed/suspected COVID-19 patients, fear of COVID-19 (no fear, moderate fear, or extreme fear), and experience of discrimination (a yes/no answer to the question, "After the COVID-19 epidemic, have you experienced discrimination in daycare centers, schools, or from community residents because you are a medical worker?") were also evaluated. In this study, we defined frontline workers as those directly involved in COVID-19 prevention and treatment and having direct contact with confirmed or suspected cases once or more than once a week.

Statistical analysis

A series of hierarchical multiple regression analyses were performed to test the effects of developmental characteristics on depression (the score of the PHQ-9) after controlling for sociodemographic factors and changes in participants' lives after the COVID-19 outbreak. First, developmental characteristics (the ASRS score and the AQ-10 score) were entered into the regression model (Model 1). Second, changes in lifestyle after the COVID-19 outbreak (changes in physical and psychological burden, changes in income, frequency of going out, and interpersonal interaction) were entered into the regression model in the second step (Model 2). Lastly, sociodemographic variables including age group, sex, BMI, residential area, number of households, habitual smoking and alcohol consumption, history of COVID-19 infection, work status (occupation, commuting time, working hours per month, engagement in night-shifts, whether a frontline worker or not), fear of COVID-19, and experience of discrimination were entered in the third and final step (Model 3). The same hierarchical multiple regression analyses were performed to test the effects of developmental characteristics on anxiety (GAD-7 score). We used SPSS statistics version 22 (SPSS Japan, Inc., Tokyo Japan) to perform all analyses. Statistical significance was set at $p<0.05$.

Patient and public involvement

There was no patient or public involvement in the production of this study.

RESULTS

The 640 participants consisted of 270 (42.2%) physicians (including dentists), 190 (29.7%) nurses (including midwives), and 180 (28.1%) other workers (pharmacists (n=34), nutritionists (n=4), radiologists (n=4), clinical technologists (n=17), physical therapists (n=6), occupational therapists (n=14), certified orthoptists (n=1), clinical engineers (n=4), speech therapists (n=8), certified care workers (n=3), clinical psychologists (n=25), psychiatric social workers (n=13), music therapists (n=1), medical assistants (n=7), and office workers (n=39)). Predominantly, the participants were in their 30s and 40s (37.3% and 34.8%, respectively), and 359 subjects (59.1%) were female. Only five participants (0.8%) had a history of COVID-19 infection. Forty-six participants (7.2%) were frontline workers. Other descriptive information of the participants is presented in Table 1. A majority of the participants (85.4%) were concerned about COVID-19, and about 20% of them were extremely fearful of COVID-19 (17.7% of all participants). Discrimination

against medical workers was experienced by 8.8% of the respondents. The prevalence of clinically significant depressive symptoms (PHQ-9≥10), anxiety symptoms (GAD-7≥10), ADHD traits (ASRS≥14) and autistic traits (AQ-10≥6) were 77 (12.0%), 54 (8.4%), 65 (10.2%), and 64 (10.0%), respectively.

Table 1. Demographic data and employment status (N=640)

Age group (years), N (%)	
20 to 29	75 (11.7)
30 to 39	239 (37.3)
40 to 49	223 (34.8)
50 to 59	74 (11.6)
≥60	29 (4.5)
Female, N (%)	359 (56.1)
Body mass index, median (IQR), kg/m2	21.8 (20.1–24.2)
Residential area, N (%)	
Urban	260 (40.6)
Suburban	279 (43.6)
Rural	101 (15.8)
Number of households, N (%)	
1	187 (29.7)
2	139 (21.7)
3	130 (20.3)
≥4	184 (28.7)
Habitual smoking, N (%)	60 (9.4)
Habitual alcohol consumption, N (%)	170 (26.6)
COVID-19 infection, N (%)	5 (0.8)
Occupation, N (%)	
Physician	270 (42.2)
Nurse	190 (29.7)
Other worker	180 (28.1)
Commuting time, N (%)	
<30 min	374 (58.4)
30 min to 1 h	183 (28.6)
≥1 h	83 (13.0)
Working hours, median (IQR), per month	207.5 (187–247)
Working night-shift, N (%)	316 (49.4)
Frontline worker, N (%)	46 (7.2)
Fear of COVID-19, N (%)	
No fear	94 (14.7)
Moderate fear	433 (67.7)
Extreme fear	113 (17.7)
Experience of discrimination, N (%)	56 (8.8)
PHQ-9 score, median (IQR), points	4 (1–8)
GAD-7 score, median (IQR), points	2 (0–5)
ASRS score, median (IQR), points	9 (6–11)
AQ-10 score, median (IQR), points	3 (2–4)

IQR, interquartile rage; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7; ASRS, Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale; AQ-10, Autism-Spectrum Quotient-10.

Changes in lifestyle (physical and psychological burden, income, frequency of going out, and

interpersonal interaction) are shown in Figure 2. In terms of workload after the COVID-19 outbreak, 49.1% and 78.3% of the participants reported that their physical and psychological burdens increased, respectively. As for income, only 19.7% of the subjects experienced a decrease below 90%. Overall, a noticeable decrease in the frequency of going out was reported—92.2% reported reducing activities by 10% or more, and 40% reported reducing their activities by 50% or more. A similar decrease in interpersonal interaction was noted, with 83.5% reporting a decrease of less than 90% and 37.7% reporting a decrease of less than 50%.

To evaluate the effect of developmental characteristics, changes in lifestyle due to COVID-19, and sociodemographic variables, we performed two separate regression analyses. For depression, the first model testing the contributions of developmental characteristics were statistically significant (R^2=21.7%, p<0.001). The addition of changes in lifestyle due to COVID-19 (Model 2) resulted in a significant increase in the R^2 value (ΔR^2=12.6%, p<0.001). The final model (the standard multiple regression analysis) in which all of the variables were entered simultaneously explained 43.3% of the variance in depression. Finally, ASRS score (β=0.390, p<0.001), AQ-10 score (β=0.069, p<0.05), changes in physical burden (β=0.121, p<0.01), changes in psychological burden (β=0.161, p<0.001), changes in interpersonal interaction (β=0.103, p<0.01), being female (β=0.199, p<0.001), body mass index (β=0.094, p<0.01), number of households (β=−0.086, p<0.01), habitual smoking (β=0.068, p<0.05), other worker (β=0.130, p<0.001), working hours per month (β=0.083, p<0.05), fear of COVID-19 (β=0.135, p<0.001), and experience of discrimination (β=0.069, p<0.05) were identified as significant correlates of depression. However, the correlation between AQ-10 score and depression was not significant in the bivariate analysis (Table 2).

Table 2. Multiple linear regression model predicting depressive symptoms*.

Predictors	Model 1			Model 2			Model 3		
	B	*SE*	*β*	*B*	*SE*	*β*	*B*	*SE*	*β*
Step 1: Developmental characteristics									
ASRS score (continuous variable)	0.562	0.043	0.463‖‖	0.508	0.04	0.418‖‖	0.474	0.039	0.390‖‖
AQ-10 score (continuous variable)	0.045	0.096	0.017	0.113	0.089	0.042	0.186	0.086	0.069‡‡
Step 2: Changes in lifestyle after the COVID-19 outbreak									
Changes in physical burden†				0.745	0.190	0.151‖‖	0.595	0.184	0.121§§
Changes in psychological burden†				1.315	0.244	0.216‖‖	0.978	0.243	0.161‖‖
Changes in income‡				−0.124	0.319	−0.013	−0.196	0.313	−0.020
Changes in frequency of going out‡				−0.324	0.277	−0.042	−0.515	0.264	−0.066
Changes in interpersonal interaction‡				0.791	0.226	0.124‖‖	0.657	0.216	0.103§§
Step 3: Sociodemographic variables									
Age group§							−0.045	0.159	−0.009
Female (yes)							1.937	0.358	0.199‖‖
Body mass index (continuous variable)							0.134	0.047	0.094§§
Residential area‖							−0.223	0.230	−0.033
Number of households¶							−0.349	0.132	−0.086§§

Habitual smoking (yes)			1.137	0.526	0.068‡‡
Habitual alcohol consumption (yes)			0.448	0.348	0.041
History of COVID-19 infection (yes)			2.021	1.693	0.037
Occupation					
Physician (reference)			—		—
Nurse			−0.131	0.425	−0.012
Other worker			1.399	0.423	0.130‖‖
Commuting time**			−0.067	0.217	−0.010
Working hours per month (continuous variable)			0.008	0.003	0.083‡‡
Working night shift (yes)			−0.099	0.343	−0.010
Frontline worker (yes)			0.233	0.602	0.012
Fear of COVID-19††			1.151	0.278	0.135‖‖
Experience of discrimination (yes)			1.176	0.548	0.069‡‡
Fit test					
R^2	0.217	0.342			0.433
Change in R^2	0.217	0.126			0.091

SE, standard error; ASRS, the Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale; AQ-10, the Autism-Spectrum Quotient-10.
*Evaluated using the Patient Health Questionnaire-9.
†markedly decreased=1, decreased=2, not changed=3, increased=4, and markedly increased=5.
‡≥150=1, 110 to 15%=2, 90 to 110%=3, 50 to 90%=4, and <50%=5.
§20 to 29=1, 30 to 39=2, 40 to 49=3, 50 to 59=4, and 60 or over 60=5.
‖urban=1, suburban=2, rural=3.
¶4 or more than 4 was calculated as '4'.
**<30 min=1, 30 min to 1 h=2, ≥1 h=3.
††No fear=1, moderate fear=2, extreme fear=3.
‡‡p<0.05, §§p<0.01, ‖‖p<0.001.

For anxiety, the first model testing the contributions of developmental characteristics were statistically significant (R^2=22.5%, p<0.001). The addition of changes in lifestyle with COVID-19 (model 2) resulted in a significant increase in the R^2 value (ΔR^2=0.105%, p<0.001). The final full model (the standard multiple regression analysis) in which all of the variables were entered simultaneously explained 39% of the variance in anxiety. Finally, the ASRS score (β=0.426, p<0.001), changes in physical burden (β=0.120, p<0.01), changes in psychological burden (β=0.146, p<0.001), being female (β=0.089, p<0.05), other worker (β=0.123, p<0.001), fear of COVID-19 (β=0.170, p<0.001), and experience of discrimination (β=0.067, p<0.05) were identified as significant correlates of anxiety (Table 3).

Table 3. Multiple linear regression model predicting anxiety symptoms*.

Predictors	Model 1			Model 2			Model 3		
	B	*SE*	*β*	*B*	*SE*	*β*	*B*	*SE*	*β*
Step 1: Developmental characteristics									
ASRS score (continuous variable)	0.480	0.036	0.472‖‖	0.438	0.034	0.431‖‖	0.433	0.033	0.426‖‖
AQ-10 score (continuous variable)	0.029	0.080	0.013	0.079	0.075	0.035	0.117	0.075	0.052
Step 2: Changes in lifestyle after the COVID-19 outbreak									
Changes in physical burden†				0.643	0.160	0.156‖‖	0.492	0.159	0.120§§
Changes in psychological burden†				0.969	0.206	0.191‖‖	0.743	0.211	0.146‖‖
Changes in income‡				0.007	0.269	0.001	−0.116	0.272	−0.014
Changes in frequency of going out‡				−0.223	0.233	−0.034	−0.257	0.229	−0.040
Changes in interpersonal interaction‡				0.507	0.190	0.095§§	0.367	0.188	0.069
Step 3: Sociodemographic variables									
Age group§							0.212	0.138	0.052
Female (yes)							0.727	0.310	0.089‡‡
Body mass index (continuous variable)							−0.015	0.040	−0.013

Residential area‖			−0.061	0.200	−0.011
Number of households¶			−0.066	0.114	−0.019
Habitual smoking (yes)			0.336	0.456	0.024
Habitual alcohol consumption (yes)			0.244	0.302	0.027
History of COVID-19 infection (yes)			1.870	1.469	0.041
Occupation					
Physician (reference)			—		—
Nurse			−0.031	0.369	−0.004
Other worker			1.108	0.367	0.123§§
Commuting time**			−0.169	0.188	−0.030
Working hours per month (continuous variable)			0.001	0.003	0.015
Working night shift (yes)			0.071	0.298	0.009
Frontline worker (yes)			0.434	0.522	0.028
Fear of COVID-19††			1.214	0.241	0.170‖‖
Experience of discrimination (yes)			0.956	0.475	0.067‡‡
Fit test					
R^2	0.225	0.330			0.390
Change in R^2	0.225	0.105			0.060

SE, standard error; ASRS, the Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale; AQ-10, the Autism-Spectrum Quotient-10.
*Evaluated using the Generalized Anxiety Disorder-7.
†markedly decreased=1, decreased=2, not changed=3, increased=4, and markedly increased=5.
‡≥150=1, 110 to 15%=2, 90 to 110%=3, 50 to 90%=4, and <50%=5.
§20 to 29=1, 30 to 39=2, 40 to 49=3, 50 to 59=4, and 60 or over 60=5.
‖urban=1, suburban=2, rural=3.
¶4 or more than 4 was calculated as '4'.
**<30 min=1, 30 min to 1 h=2, ≥1 h=3.
††No fear=1, moderate fear=2, extreme fear=3.
‡‡p<0.05, §§p<0.01, ‖‖p<0.001.

DISCUSSION

This is the first study investigating the influence of developmental characteristics on depression and anxiety in medical workers after the COVID-19 outbreak. Results indicated that ADHD traits might have a strong influence on depression and anxiety symptoms even after controlling for physical and psychological burden and fear of COVID-19, with its effect possibly being greater than other factors, including autistic traits.

In general, and not only during a pandemic, the relationship between ADHD and depression or anxiety has already been addressed.[34-39] Additionally, in general, ASD patients are more prone to develop depression and anxiety.[40] However, in this study, wherein a strong correlation was found between ADHD traits and depression/anxiety symptoms, there was no significant correlation for autistic traits. The difference in the association between the two traits for depression/anxiety is not clear. One possible reason for the strong correlation between ADHD traits and depression/anxiety is that people with ADHD traits may have faced a higher risk of infection due to their own inattention and impulsivity, which can be an obvious stressor among medical workers. Further, due to the calls for self-restraint by government leaders,[14] those with high ADHD traits may have experienced high stress;[41] self-restraint prevents one from engaging in a variety of activities,

and it would be difficult for people with ADHD traits to adapt to such activities even after months or years. Meanwhile, people with autistic traits may have shown some level of adaption to the situation, as the survey was conducted more than 6 months after the COVID-19 outbreak. Furthermore, unnecessary outings or interpersonal interactions, which can be stressors for people with autistic traits,[42] have been reduced due to COVID-19. It is also noteworthy that the correlation between autistic traits and depression, which was not significant in the bivariate analysis, was significant in the multivariate analysis. This makes it undeniable that autistic traits are also a unique factor that can be associated with depression. From the above results, it can be inferred that the relationship between psychological burden and ADHD or autistic traits after the COVID-19 outbreak should be evaluated and further investigated not only among health care workers but also among the general population. Contrary to the above hypothesis that reducing unnecessary interpersonal interaction could be protective for individuals with autistic traits, this study highlighted the importance of maintaining interpersonal interactions to fight depression. Both belonging to a large household and maintaining interpersonal interactions had a protective effect against depression symptoms. This result is consistent with the known importance of receiving direct social support from friends, family, colleagues, and supervisors during a pandemic, which has already been suggested in numerous studies.[3 4 7-9 11] In this study, the association between changes in interpersonal interaction and anxiety symptoms was not significant; this may be because reduced interpersonal interaction may lower the risk of infection and could thus reduce anxiety. Contrarily, the experience of discriminatory treatment was independently associated with both depression and anxiety symptoms. The negative psychological impact of discrimination on health care workers has been reported in previous pandemics, such as severe acute respiratory syndrome, Middle East respiratory syndrome, or other viral infections.[3 4] This study's results are consistent with the findings of the COVID-19 outbreak, which also revealed the incidence of mental disorders due to discrimination. [43-46]

Factors related to employment can also be a psychological burden for medical workers. We found that the physical and psychological burden of the COVID-19 outbreak was increased in around 50% and 80% of medical workers, respectively. Both increases in psychological and physical burden were independently associated with symptoms of depression and anxiety, which is consistent with previous studies.[47 48] It has also been reported that protective garments can increase physical burden[49 50] and that strict infection control measures can increase stress levels.[47] In addition to changes in physical and psychological burden, long

working hours were significantly correlated with depression symptoms in this study. This confirms that the long working hours of nurses were associated with increased stress under the COVID-19 outbreak.[51] Furthermore, a significant association between the fear of COVID-19, depression, and anxiety has been replicated, which is consistent with previous study findings.[2 4 9] Despite the increased psychological and physical burden and fear of COVID-19, the prevalence of clinically significant symptoms of depression and anxiety was lower than among health care workers in other nations. [6 8 12 52] This may reflect the low number of dominant COVID-19 patients and the low number of deaths due to COVID-19 in Japan as compared to other countries.[13] In addition, the low prevalence of clinically significant symptoms of depression and anxiety could be attributed to the current study's small sample of medical workers who had direct contact with COVID-19 patients compared to the sample size in previously conducted studies.[10-12 53 54] Besides, unlike previous reports on the general population,[55-58] the association between the income loss associated with the COVID-19 outbreak, depression, and anxiety was not clear in this study. This can be due to the limited number of medical workers who experienced a decline in income; the impact could be greater if the economy had collapsed, and their incomes had drastically decreased.

The current results suggested that, remarkably, medical workers other than physicians or nurses have an independent risk of both depression and anxiety. In terms of occupation, although frontline physicians had a higher incidence of depression than other occupations,[52] a number of studies on health care workers have reported lower depression and anxiety in physicians than in other occupations,[3 4 6-8 12] as in this study. For health care workers other than physicians and nurses, one study reported that anxiety was significantly higher, but depression was comparable.[59] Another study conducted on a cruise ship during the early stages of the COVID-19 epidemic in Japan reported that distress was significantly stronger among clerical workers than physicians or nurses,[60] which are consistent with the results of the current study. Even in health care workers, inadequate medical knowledge was reported to be associated with increased levels of anxiety and depression.[3 61 62] Moreover, numerous reports have stated that fewer years of health care experience was associated with worse mental health outcomes;[3 6] other medical workers in this study may have had less experience in infection prevention. Therefore, both job-specific support and appropriate knowledge development would be important to improve the psychological burden of medical workers.

In terms of demographic variables, being female, BMI, and smoking habits were independently

associated with depression symptoms. Being female was also independently associated with anxiety symptoms. The association between BMI, smoking habits, and depression has long been shown in the general population[63 64] and may not be unique to the COVID-19 outbreak. The association of sex, especially being a woman with depression and anxiety, has been reported in a number of studies conducted on health care workers after the onset of the COVID-19 pandemic.[2-4 7 11 12 21 40] This may also reflect the higher prevalence of depression and anxiety among women in the general population;[65 66] however, these relationships can be unique to the COVID-19 pandemic. Experimental studies have shown that women are more responsive to neural networks associated with fear and arousal responses than men;[67] the response to fear associated with COVID-19 may have been stronger in women than men. In addition, there are indications that the sociological burden on women has increased after the COVID-19 outbreak.[68] Moreover, a longitudinal study of women with children showed that depression and anxiety were higher among women who had disrupted income, difficulty balancing work and family education, and difficulty obtaining daycare.[69] Indeed, in Japan, it has been reported that suicide among women increased significantly after the COVID-19 outbreak.[70] The direct causes of depression and anxiety in females, and what interventions are best for them should be examined in the future.

There are some limitations to this study. First, the present study adopted the snowball sampling strategy. While this approach is valuable for exploratory studies and provides access to the target population, it can hinder the generalizability of results as the representativeness of the sample is not guaranteed. Second, the participants with ADHD or autistic traits in this study were not formally diagnosed as having ADHD or ASD. In addition, determining whether they are traits or symptoms can be difficult using the questionnaire method. Third, the study only examined the changes in income, frequency of going out, and interpersonal interaction, and did not assess baseline status. In particular, we did not investigate economic status, which is thought to strongly influence depression and anxiety. As this study included people working in medical institutions, it may have been biased toward middle- and high-income populations in Japan.

The present study suggested that individual developmental characteristics, especially ADHD traits, have a considerable effect on the psychological health of medical workers. In contrast, the relationship between autistic traits and depression/anxiety symptoms was less significant. Identifying stressors in medical workers with high ADHD traits and the subsequent development of appropriate interventions for them are

warranted. Additionally, the relationship between specific developmental characteristics and stress-related outcomes should be replicated in further studies with both health care workers and the general population.

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Contributors

KM, RO, NA, and MH had full access to all of the data and took responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: KM, TY, AT, KN, TU, KY, and KK. Acquisition, analysis or interpretation of data: all authors. Drafting of the manuscript: KM. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: KM. Obtained funding: KM. Supervision: TY, MF, KK. All authors have contributed significantly to this work and have met the qualification of authorship.

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Competing interests

None declared.

Ethics approval

The study protocol was approved by the ethical committee of the National Center of Neurology and Psychiatry (A2020-044).

Data availability statement

The data that support the findings of this study are available from the corresponding author on reasonable

request.

REFERENCES

1. Chew QH, Wei KC, Vasoo S, et al. Psychological and Coping Responses of Health Care Workers Toward Emerging Infectious Disease Outbreaks: A Rapid Review and Practical Implications for the COVID-19 Pandemic. *The Journal of clinical psychiatry* 2020;81(6) doi: 10.4088/JCP.20r13450 [published Online First: 2020/10/22]
2. Serrano-Ripoll MJ, Meneses-Echavez JF, Ricci-Cabello I, et al. Impact of viral epidemic outbreaks on mental health of healthcare workers: a rapid systematic review and meta-analysis. *Journal of affective disorders* 2020;277:347-57. doi: 10.1016/j.jad.2020.08.034 [published Online First: 2020/08/31]
3. Sirois FM, Owens J. Factors Associated With Psychological Distress in Health-Care Workers During an Infectious Disease Outbreak: A Rapid Systematic Review of the Evidence. *Frontiers in psychiatry* 2020;11:589545. doi: 10.3389/fpsyt.2020.589545 [published Online First: 2021/02/16]
4. Cabarkapa S, Nadjidai SE, Murgier J, et al. The psychological impact of COVID-19 and other viral epidemics on frontline healthcare workers and ways to address it: A rapid systematic review. *Brain, behavior, & immunity - health* 2020;8:100144. doi: 10.1016/j.bbih.2020.100144 [published Online First: 2020/09/23]
5. Xiang YT, Yang Y, Li W, et al. Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed. *The lancet Psychiatry* 2020;7(3):228-29. doi: 10.1016/s2215-0366(20)30046-8 [published Online First: 2020/02/08]
6. Sanghera J, Pattani N, Hashmi Y, et al. The impact of SARS-CoV-2 on the mental health of healthcare workers in a hospital setting-A Systematic Review. *Journal of occupational health* 2020;62(1):e12175. doi: 10.1002/1348-9585.12175 [published Online First: 2020/11/02]
7. Pappa S, Ntella V, Giannakas T, et al. Prevalence of depression, anxiety, and insomnia among healthcare workers during the COVID-19 pandemic: A systematic review and meta-analysis. *Brain, behavior, and immunity* 2020;88:901-07. doi: 10.1016/j.bbi.2020.05.026 [published Online First: 2020/05/22]
8. Luo M, Guo L, Yu M, et al. The psychological and mental impact of coronavirus disease 2019 (COVID-19) on medical staff and general public - A systematic review and meta-analysis. *Psychiatry research* 2020;291:113190. doi: 10.1016/j.psychres.2020.113190 [published Online First: 2020/06/22]
9. Muller AE, Hafstad EV, Himmels JPW, et al. The mental health impact of the covid-19 pandemic on healthcare workers, and interventions to help them: A rapid systematic review. *Psychiatry research* 2020;293:113441. doi: 10.1016/j.psychres.2020.113441 [published Online First: 2020/09/09]
10. da Silva FCT, Neto MLR. Psychiatric symptomatology associated with depression, anxiety, distress, and insomnia in health professionals working in patients affected by COVID-19: A systematic review with meta-analysis. *Progress in neuro-psychopharmacology & biological psychiatry* 2021;104:110057. doi: 10.1016/j.pnpbp.2020.110057 [published Online First: 2020/08/11]
11. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: Systematic review of the current evidence. *Brain, behavior, and immunity* 2020;89:531-42. doi: 10.1016/j.bbi.2020.05.048 [published Online First: 2020/06/03]
12. Vizheh M, Qorbani M, Arzaghi SM, et al. The mental health of healthcare workers in the COVID-19 pandemic: A systematic review. *Journal of diabetes and metabolic disorders* 2020:1-12. doi: 10.1007/s40200-020-00643-9 [published Online First: 2020/11/03]
13. Johns Hopkins University. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE). Available from: https:coronavirus.jhu.edu/map.htmlhttps:coronavirus.jhu.edu/map.html. [Accessed 15 Feb 2021].

14. Tokumoto A, Akaba H, Oshitani H, et al. COVID-19 Health system response monitor: Japan. New Delhi: World Health Organization. Regional Office for South-East Asia 2020.
15. Furuse Y, Sando E, Tsuchiya N, et al. Clusters of Coronavirus Disease in Communities, Japan, January-April 2020. *Emerging infectious diseases* 2020;26(9):2176-9. doi: 10.3201/eid2609.202272 [published Online First: 2020/06/11]
16. Rotenstein LS, Torre M, Ramos MA, et al. Prevalence of Burnout Among Physicians: A Systematic Review. *Jama* 2018;320(11):1131-50. doi: 10.1001/jama.2018.12777 [published Online First: 2018/10/17]
17. Colizzi M, Sironi E, Antonini F, et al. Psychosocial and Behavioral Impact of COVID-19 in Autism Spectrum Disorder: An Online Parent Survey. *Brain sciences* 2020;10(6) doi: 10.3390/brainsci10060341 [published Online First: 2020/06/07]
18. Melegari MG, Giallonardo M, Sacco R, et al. Identifying the impact of the confinement of Covid-19 on emotional-mood and behavioural dimensions in children and adolescents with attention deficit hyperactivity disorder (ADHD). *Psychiatry research* 2020;296:113692. doi: 10.1016/j.psychres.2020.113692 [published Online First: 2021/01/10]
19. Bobo E, Lin L, Acquaviva E, et al. [How do children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD) experience lockdown during the COVID-19 outbreak?]. *L'Encephale* 2020;46(3s):S85-s92. doi: 10.1016/j.encep.2020.05.011 [published Online First: 2020/06/12]
20. Sciberras E, Patel P, Stokes MA, et al. Physical Health, Media Use, and Mental Health in Children and Adolescents With ADHD During the COVID-19 Pandemic in Australia. *Journal of attention disorders* 2020:1087054720978549. doi: 10.1177/1087054720978549 [published Online First: 2020/12/18]
21. Mutluer T, Doenyas C, Aslan Genc H. Behavioral Implications of the Covid-19 Process for Autism Spectrum Disorder, and Individuals' Comprehension of and Reactions to the Pandemic Conditions. *Frontiers in psychiatry* 2020;11:561882. doi: 10.3389/fpsyt.2020.561882 [published Online First: 2020/12/12]
22. Amorim R, Catarino S, Miragaia P, et al. The impact of COVID-19 on children with autism spectrum disorder. *Revista de neurologia* 2020;71(8):285-91. doi: 10.33588/rn.7108.2020381 [published Online First: 2020/10/10]
23. Antshel KM, Russo N. Autism Spectrum Disorders and ADHD: Overlapping Phenomenology, Diagnostic Issues, and Treatment Considerations. *Current psychiatry reports* 2019;21(5):34. doi: 10.1007/s11920-019-1020-5 [published Online First: 2019/03/25]
24. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine* 2001;16(9):606-13. doi: 10.1046/j.1525-1497.2001.016009606.x [published Online First: 2001/09/15]
25. Muramatsu K, Miyaoka H, Kamijima K, et al. Performance of the Japanese version of the Patient Health Questionnaire-9 (J-PHQ-9) for depression in primary care. *General hospital psychiatry* 2018;52:64-69. doi: 10.1016/j.genhosppsych.2018.03.007 [published Online First: 2018/04/27]
26. Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Archives of internal medicine* 2006;166(10):1092-7. doi: 10.1001/archinte.166.10.1092 [published Online First: 2006/05/24]
27. Validation and utility of a Japanese version of the GAD-7 2009.
28. Kessler RC, Adler L, Ames M, et al. The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. *Psychological medicine* 2005;35(2):245-56. doi: 10.1017/s0033291704002892 [published Online First: 2005/04/22]

29. Kessler RC, Adler LA, Gruber MJ, et al. Validity of the World Health Organization Adult ADHD Self-Report Scale (ASRS) Screener in a representative sample of health plan members. *International journal of methods in psychiatric research* 2007;16(2):52-65. doi: 10.1002/mpr.208 [published Online First: 2007/07/12]

30. Baron-Cohen S, Wheelwright S, Skinner R, et al. The autism-spectrum quotient (AQ): evidence from Asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. *Journal of autism and developmental disorders* 2001;31(1):5-17. doi: 10.1023/a:1005653411471 [published Online First: 2001/07/07]

31. Kurita H, Koyama T, Osada H. Autism-Spectrum Quotient-Japanese version and its short forms for screening normally intelligent persons with pervasive developmental disorders. *Psychiatry and clinical neurosciences* 2005;59(4):490-6. doi: 10.1111/j.1440-1819.2005.01403.x [published Online First: 2005/07/29]

32. American Psychiatric Association. DSM-IV: Diagnostic and statistical manual (Fourth Edition). Washington, DC: American Psychiatric Association 1994.

33. Lundin A, Kosidou K, Dalman C. Measuring Autism Traits in the Adult General Population with the Brief Autism-Spectrum Quotient, AQ-10: Findings from the Stockholm Public Health Cohort. *Journal of autism and developmental disorders* 2019;49(2):773-80. doi: 10.1007/s10803-018-3749-9 [published Online First: 2018/09/24]

34. Nankoo MMA, Palermo R, Bell JA, et al. Examining the Rate of Self-Reported ADHD-Related Traits and Endorsement of Depression, Anxiety, Stress, and Autistic-Like Traits in Australian University Students. *Journal of attention disorders* 2019;23(8):869-86. doi: 10.1177/1087054718758901 [published Online First: 2018/03/06]

35. Combs MA, Canu WH, Broman-Fulks JJ, et al. Perceived stress and ADHD symptoms in adults. *Journal of attention disorders* 2015;19(5):425-34. doi: 10.1177/1087054712459558 [published Online First: 2012/10/05]

36. Evren B, Evren C, Dalbudak E, et al. The impact of depression, anxiety, neuroticism, and severity of Internet addiction symptoms on the relationship between probable ADHD and severity of insomnia among young adults. *Psychiatry research* 2019;271:726-31. doi: 10.1016/j.psychres.2018.12.010 [published Online First: 2019/02/23]

37. Shen Y, Zhang Y, Chan BSM, et al. Association of ADHD symptoms, depression and suicidal behaviors with anxiety in Chinese medical college students. *BMC Psychiatry* 2020;20(1):180. doi: 10.1186/s12888-020-02555-7 [published Online First: 2020/04/24]

38. Mohamed SMH, Börger NA, van der Meere JJ. Executive and Daily Life Functioning Influence the Relationship Between ADHD and Mood Symptoms in University Students. *Journal of attention disorders* 2020:1087054719900251. doi: 10.1177/1087054719900251 [published Online First: 2020/01/24]

39. Oh Y, Yoon HJ, Kim JH, et al. Trait Anxiety as a Mediator of the Association between Attention Deficit Hyperactivity Disorder Symptom Severity and Functional Impairment. *Clinical psychopharmacology and neuroscience : the official scientific journal of the Korean College of Neuropsychopharmacology* 2018;16(4):407-14. doi: 10.9758/cpn.2018.16.4.407 [published Online First: 2018/11/24]

40. Hollocks MJ, Lerh JW, Magiati I, et al. Anxiety and depression in adults with autism spectrum disorder: a systematic review and meta-analysis. *Psychological medicine* 2019;49(4):559-72. doi: 10.1017/s0033291718002283 [published Online First: 2018/09/05]

41. Jarrett MA. Attention-deficit/hyperactivity disorder (ADHD) symptoms, anxiety symptoms, and executive functioning in emerging adults. *Psychological assessment* 2016;28(2):245-50. doi: 10.1037/pas0000190 [published Online First: 2015/06/30]

42. Howlin P, Magiati I. Autism spectrum disorder: outcomes in adulthood. *Current opinion in psychiatry* 2017;30(2):69-76. doi: 10.1097/yco.0000000000000308 [published Online First: 2017/01/10]

43. Rana W, Mukhtar S, Mukhtar S. Mental health of medical workers in Pakistan during the pandemic COVID-19 outbreak. *Asian journal of psychiatry* 2020;51:102080. doi: 10.1016/j.ajp.2020.102080 [published Online First: 2020/04/14]

44. Singh R, Subedi M. COVID-19 and stigma: Social discrimination towards frontline healthcare providers and COVID-19 recovered patients in Nepal. *Asian journal of psychiatry* 2020;53:102222-22. doi: 10.1016/j.ajp.2020.102222 [published Online First: 2020/06/13]

45. Abdel Wahed WY, Hefzy EM, Ahmed MI, et al. Assessment of Knowledge, Attitudes, and Perception of Health Care Workers Regarding COVID-19, A Cross-Sectional Study from Egypt. *J Community Health* 2020;45(6):1242-51. doi: 10.1007/s10900-020-00882-0

46. Chatterjee SS, Bhattacharyya R, Bhattacharyya S, et al. Attitude, practice, behavior, and mental health impact of COVID-19 on doctors. *Indian journal of psychiatry* 2020;62(3):257-65. doi: 10.4103/psychiatry.IndianJPsychiatry_333_20 [published Online First: 2020/08/11]

47. Zhang C, Yang L, Liu S, et al. Survey of Insomnia and Related Social Psychological Factors Among Medical Staff Involved in the 2019 Novel Coronavirus Disease Outbreak. *Frontiers in psychiatry* 2020;11:306. doi: 10.3389/fpsyt.2020.00306 [published Online First: 2020/04/30]

48. Du J, Dong L, Wang T, et al. Psychological symptoms among frontline healthcare workers during COVID-19 outbreak in Wuhan. *General hospital psychiatry* 2020;67:144-45. doi: 10.1016/j.genhosppsych.2020.03.011 [published Online First: 2020/05/10]

49. Epstein Y, Heled Y, Ketko I, et al. The effect of air permeability characteristics of protective garments on the induced physiological strain under exercise-heat stress. *The Annals of occupational hygiene* 2013;57(7):866-74. doi: 10.1093/annhyg/met003 [published Online First: 2013/02/05]

50. Davey SL, Lee BJ, Robbins T, et al. Heat stress and PPE during COVID-19: impact on healthcare workers' performance, safety and well-being in NHS settings. *The Journal of hospital infection* 2021;108:185-88. doi: 10.1016/j.jhin.2020.11.027 [published Online First: 2020/12/11]

51. Mo Y, Deng L, Zhang L, et al. Work stress among Chinese nurses to support Wuhan in fighting against COVID-19 epidemic. *Journal of nursing management* 2020;28(5):1002-09. doi: 10.1111/jonm.13014 [published Online First: 2020/04/08]

52. Salari N, Khazaie H, Hosseinian-Far A, et al. The prevalence of stress, anxiety and depression within front-line healthcare workers caring for COVID-19 patients: a systematic review and meta-regression. *Human resources for health* 2020;18(1):100. doi: 10.1186/s12960-020-00544-1 [published Online First: 2020/12/19]

53. Lai J, Ma S, Wang Y, et al. Factors Associated With Mental Health Outcomes Among Health Care Workers Exposed to Coronavirus Disease 2019. *JAMA network open* 2020;3(3):e203976. doi: 10.1001/jamanetworkopen.2020.3976 [published Online First: 2020/03/24]

54. Lu W, Wang H, Lin Y, et al. Psychological status of medical workforce during the COVID-19 pandemic: A cross-sectional study. *Psychiatry research* 2020;288:112936. doi: 10.1016/j.psychres.2020.112936 [published Online First: 2020/04/11]

55. Fukase Y, Ichikura K, Murase H, et al. Depression, risk factors, and coping strategies in the context of social

dislocations resulting from the second wave of COVID-19 in Japan. *BMC Psychiatry* 2021;21(1):33. doi: 10.1186/s12888-021-03047-y [published Online First: 2021/01/14]

56. Kuang Y, Shen M, Wang Q, et al. Association of outdoor activity restriction and income loss with patient-reported outcomes of psoriasis during the COVID-19 pandemic: A web-based survey. *Journal of the American Academy of Dermatology* 2020;83(2):670-72. doi: 10.1016/j.jaad.2020.05.018 [published Online First: 2020/05/15]
57. Shevlin M, McBride O, Murphy J, et al. Anxiety, depression, traumatic stress and COVID-19-related anxiety in the UK general population during the COVID-19 pandemic. *BJPsych open* 2020;6(6):e125. doi: 10.1192/bjo.2020.109 [published Online First: 2020/10/20]
58. Witteveen D, Velthorst E. Economic hardship and mental health complaints during COVID-19. *Proceedings of the National Academy of Sciences of the United States of America* 2020;117(44):27277-84. doi: 10.1073/pnas.2009609117 [published Online First: 2020/10/14]
59. Tan BYQ, Chew NWS, Lee GKH, et al. Psychological Impact of the COVID-19 Pandemic on Health Care Workers in Singapore. *Annals of internal medicine* 2020;173(4):317-20. doi: 10.7326/m20-1083 [published Online First: 2020/04/07]
60. Ide K, Asami T, Suda A, et al. The psychological effects of COVID-19 on hospital workers at the beginning of the outbreak with a large disease cluster on the Diamond Princess cruise ship. *PloS one* 2021;16(1):e0245294. doi: 10.1371/journal.pone.0245294 [published Online First: 2021/01/12]
61. Cag Y, Erdem H, Gormez A, et al. Anxiety among front-line health-care workers supporting patients with COVID-19: A global survey. *General hospital psychiatry* 2021;68:90-96. doi: 10.1016/j.genhosppsych.2020.12.010 [published Online First: 2021/01/09]
62. García-Fernández L, Romero-Ferreiro V, López-Roldán PD, et al. Mental health impact of COVID-19 pandemic on Spanish healthcare workers. *Psychological medicine* 2020:1-3. doi: 10.1017/s0033291720002019 [published Online First: 2020/05/28]
63. Anda RF, Williamson DF, Escobedo LG, et al. Depression and the dynamics of smoking. A national perspective. *Jama* 1990;264(12):1541-5. [published Online First: 1990/09/26]
64. de Wit L, Luppino F, van Straten A, et al. Depression and obesity: a meta-analysis of community-based studies. *Psychiatry research* 2010;178(2):230-5. doi: 10.1016/j.psychres.2009.04.015 [published Online First: 2010/05/14]
65. Piccinelli M, Wilkinson G. Gender differences in depression. Critical review. *Br J Psychiatry* 2000;177:486-92. doi: 10.1192/bjp.177.6.486 [published Online First: 2000/12/05]
66. McLean CP, Asnaani A, Litz BT, et al. Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. *Journal of psychiatric research* 2011;45(8):1027-35. doi: 10.1016/j.jpsychires.2011.03.006 [published Online First: 2011/03/29]
67. Felmingham K, Williams LM, Kemp AH, et al. Neural responses to masked fear faces: sex differences and trauma exposure in posttraumatic stress disorder. *Journal of abnormal psychology* 2010;119(1):241-7. doi: 10.1037/a0017551 [published Online First: 2010/02/10]
68. McLaren HJ, Wong KR, Nguyen KN, et al. Covid-19 and women's triple burden: Vignettes from Sri Lanka, Malaysia, Vietnam and Australia. *Social Sciences* 2020;9(5):87.
69. Racine N, Hetherington E, McArthur BA, et al. Maternal depressive and anxiety symptoms before and during the COVID-19 pandemic in Canada: a longitudinal analysis. *The lancet Psychiatry* 2021 doi: 10.1016/s2215-0366(21)00074-2 [published Online First: 2021/03/28]

70. Nomura S, Kawashima T, Yoneoka D, et al. Trends in suicide in Japan by gender during the COVID-19 pandemic, up to September 2020. *Psychiatry research* 2021;295:113622. doi: 10.1016/j.psychres.2020.113622 [published Online First: 2020/12/09]

Figure Legends

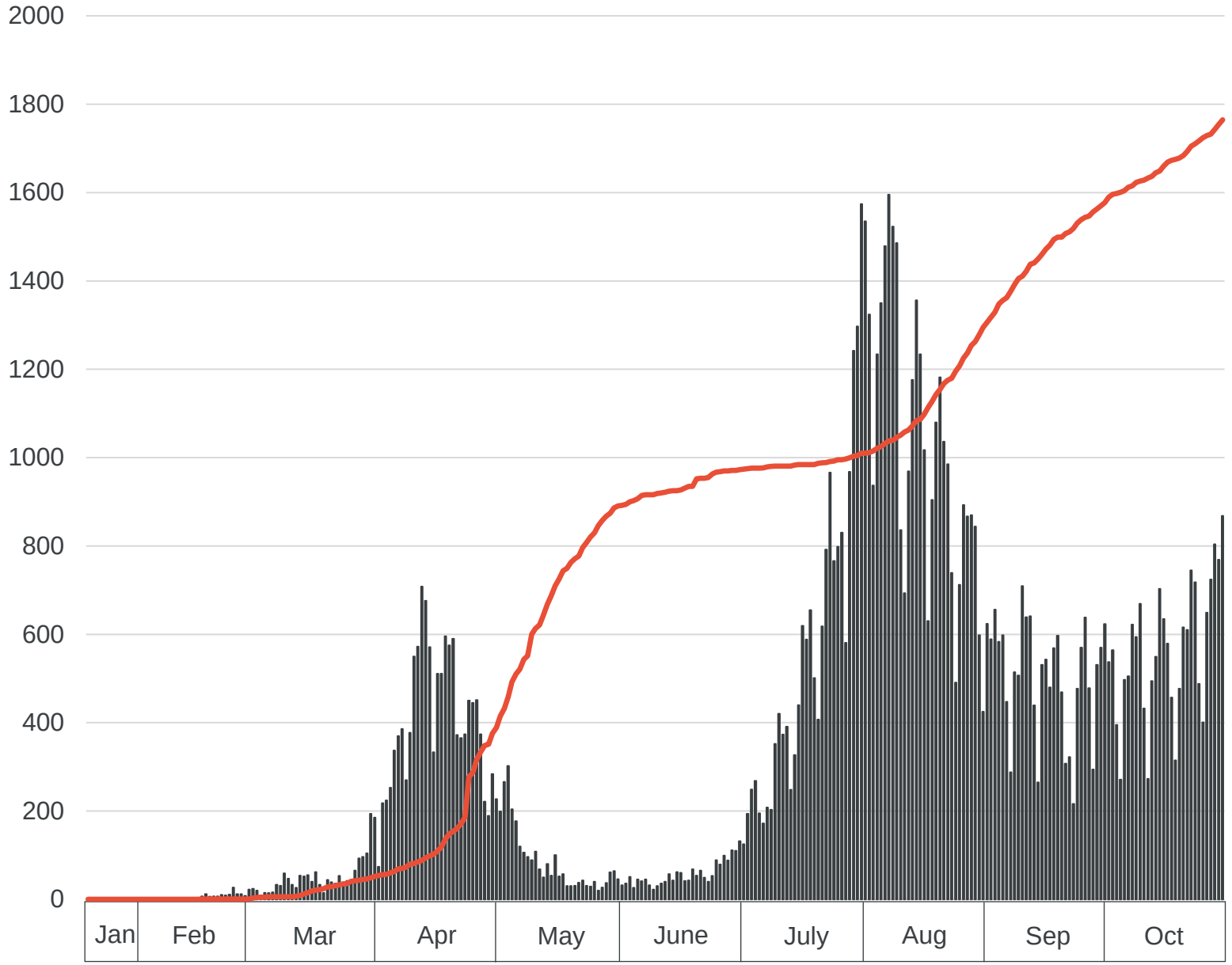
Figure 1. Epidemic curve of COVID-19 in Japan until October 2020

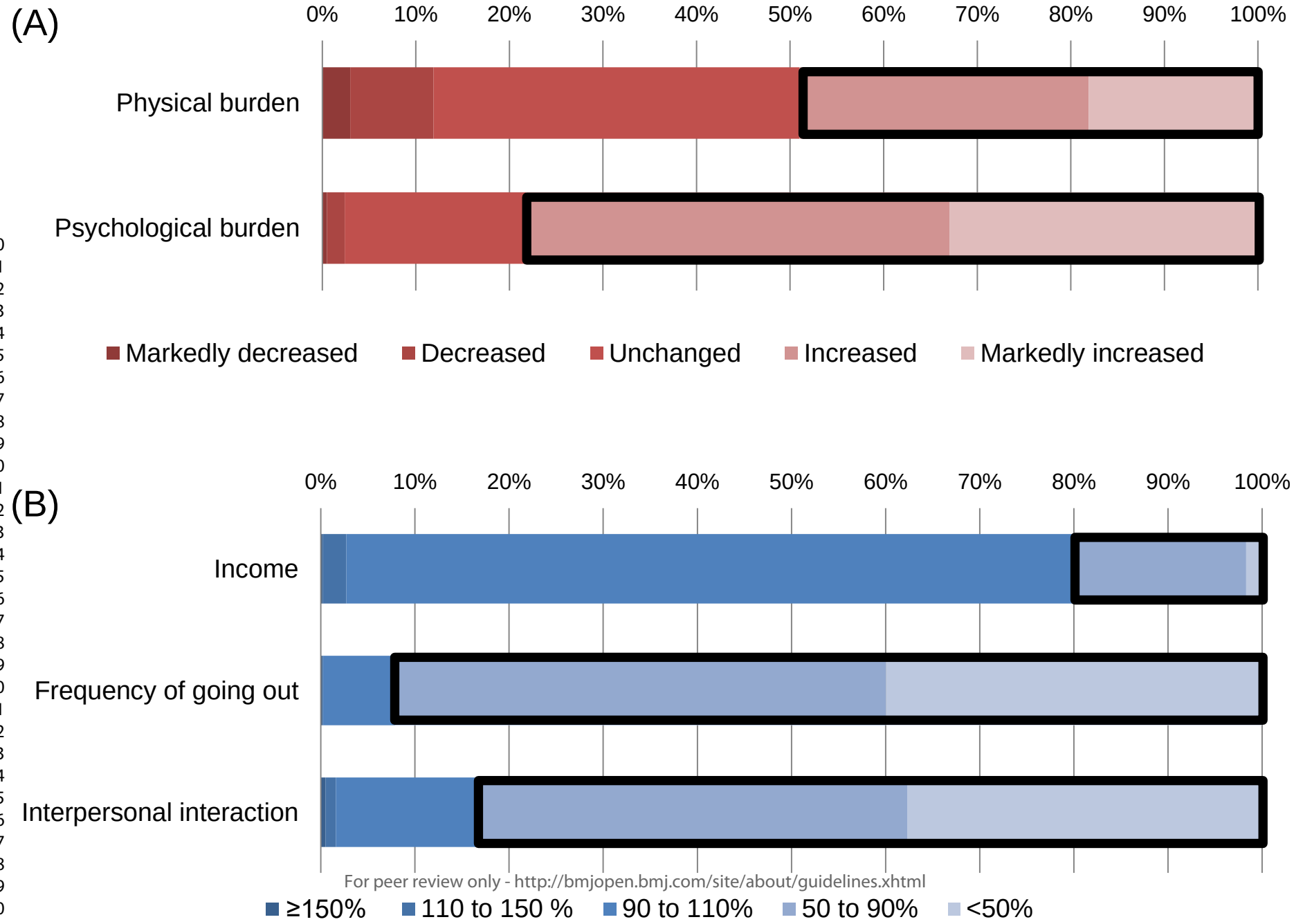
The bar graph shows the epidemic curve displaying the number of patients. The red line shows the cumulative number of deaths.

Figure 2. Changes in lifestyle among medical workers after the COVID-19 outbreak

(A) The bold square shows an increase in physical and psychological burden.

(B) The bold square shows a decrease of less than 90%.





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The Psychological Burden of Attention-Deficit/Hyperactivity Disorder Traits on Medical Workers Under the COVID-19 Outbreak: A Cross-Sectional Web-Based Questionnaire Survey

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ABSTRACT

Objectives:

There are numerous reports on the psychological burden of medical workers after the COVID-19 outbreak; however, no study has examined the influence of developmental characteristics on the mental health of medical workers. The objective of this study was to examine whether the developmental characteristics of medical workers are associated with anxiety and depression after the COVID-19 outbreak.

Design:

We conducted an online cross-sectional questionnaire survey in October 2020.

Participants and setting:

The data of 640 medical workers were analyzed. The questionnaire included items on sociodemographic data, changes in their life after the COVID-19 outbreak, and symptoms of depression, anxiety, attention deficit/hyperactivity disorder (ADHD) traits, and autism spectrum disorder traits.

Main outcomes:

Depression symptoms were assessed by the Patient Health Questionnaire-9 (PHQ-9) and anxiety symptoms were assessed by the Generalized Anxiety Disorder-7 (GAD-7). A series of hierarchical multiple regression analyses were performed to test the effects of developmental characteristics on depression and anxiety symptoms after controlling for sociodemographic factors and changes in participants' lives after the COVID-19 outbreak.

Results:

Increases in physical and psychological burden were observed in 49.1% and 78.3% of the subjects, respectively. The results of a multiple regression analysis showed that ADHD traits were significantly

associated with both depression (β=0.390, p<0.001) and anxiety (β=0.426, p<0.001). Autistic traits were significantly associated with depression (β=0.069, p<0.05) but not anxiety. Increased physical and psychological burden, being female, medical workers other than physicians and nurses, fear of COVID-19, and experience of discrimination were also significantly associated with both depression and anxiety.

Conclusion:

Globally, the burden on medical workers increased. This study suggested that medical workers with higher ADHD traits may need special attention during the COVID-19 pandemic.

ARTICLE SUMMARY

Strengths and Limitations of this study:

- First study to examine the association between developmental characteristics and psychological burden of medical workers under the COVID-19 outbreak.
- Sufficiently large sample size.
- Broad assessment on occupational environment and the changes in daily lifestyle under the COVID-19 outbreak.
- Despite an attempt to obtain a diverse sample of medical workers, the sample was skewed toward certain professions.
- Developmental characteristics in this study were not formal diagnoses.

INTRODUCTION

Previous studies have shown that outbreaks of serious infectious diseases can place a heavy psychological burden on health care workers.[1-5] Immediately after the coronavirus disease 2019 (COVID-19) outbreak, it was pointed out that mental health problems can emerge among medical workers due to the fear of risking infection to their own family, friends, and colleagues, with uncertainty about the future, and stigmatization of themselves.[6] There have already been a number of studies reporting mental health problems among health care workers working against COVID-19.[1-4 7-29] However, these reports were mainly from regions such as China, the United States, and European countries that experienced severe consequences of the COVID-19 pandemic.

Compared to the above-mentioned countries, the number of new cases and deaths caused by COVID-19 in Japan was small (Figure 1);[30] hence, people experiencing loss through death were considered rare. Although there has been no government-imposed lockdown with legal restraints, the further spread of COVID-19 has been prevented by only a request for self-restraint in social activities by the Prime Minister and prefectural governors.[31] People's compliance with the request of wearing masks and avoiding unnecessary outings might have contributed to preventing the spread of the disease, but their effectiveness are not clear. In contrast, medical institutes, along with restaurants/bars and music events, were reported to have contributed to cluster outbreaks,[32] leading to increased stigma and discrimination against health care workers. Thus, it is not only the fear of infection by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), but also the increased workload related to infection control, stigma/discrimination, and stress in health care workers. When health care workers experience physical or mental health problems, it could lead to a decline in health care services and ultimately affect patients.[33] As maintaining the quality of health care services affects the interests of society as a whole, reducing the physical and mental burden of health care providers would be the most essential factor to overcome the COVID-19 pandemic.

People with specific developmental characteristics may experience greater psychological burden during the COVID-19 pandemic.[15 34-38] However, there have been no reports on the psychological effects of the COVID-19 pandemic on adult health care workers with attention-deficit hyperactivity disorder (ADHD) and/or autistic traits. In recent years, ADHD and autistic traits have been regarded as spectra and have been shown to co-occur.[39] ADHD traits may make compliance with the COVID-19 precautions highly stressful; the increased risk of infection due to symptoms such as inattention, hyperactivity, and impulsivity can put the individuals and their families in danger and may also promote discrimination. Previous studies have shown that untreated ADHD is a risk factor for acquiring COVID-19.[40 41] Meanwhile, autism spectrum disorder (ASD) is characterized by intolerance to change and overestimation of variability in the surrounding environment.[42] Therefore, autistic traits may make people vulnerable to depression and anxiety because of the need to adjust their daily lifestyles to the COVID-19 crisis. Considering this, we hypothesized that medical workers with developmental characteristics such as ADHD and autistic traits experience depression and anxiety symptoms to a greater extent during the COVID-19 outbreak. In testing this hypothesis, we conducted a cross-sectional study to examine the relationship between developmental characteristics and depressive/anxiety symptoms. We included COVID-19-related changes in lifestyle, changes in psychological and physical burdens of work, and current work status based on recent findings on COVID-19 and the psychological burden of healthcare workers[2-4 8-10 12 13 15-29], as well as the possibility of an association between individuals' developmental characteristics evaluated using questionnaires as potential confounders. Our goal was to estimate the impact of ADHD and autism traits on depressive and anxiety symptoms in medical workers; however, we also discussed the effects of other factors as secondary outcomes.

METHODS

Setting and study population

The present study was conducted as part of a comprehensive research project [MEdical Workers'

MEntal health and Working conditions in Japan under the COVID-19 pandemic (MEW2-J-COVID) project] to investigate the mental health, work, lifestyle, and distraction of medical workers after the COVID-19 outbreak. This cross-sectional web-based questionnaire survey was conducted between October 1 and 30, 2020. Participants were recruited via snowball sampling. The method of dissemination was not specified; potential participants were asked to access the link to a Google Form containing the questionnaire posted on the National Center of Neurology and Psychiatry website. Informed consent was obtained from all participants via the survey website.

Of the 712 participants who completed the Google Form questionnaire, the data of 683 participants were analyzed. Data of 29 participants were excluded because they were duplicates (n=24), were under 20 years or not medical workers (n=3), contained garbled data (n=1), or contained invalid data on working hours (n=1). Of these, those not working at a medical institution (n=25) and working less than 15 days in a month (n=18) were excluded. Totally, 43 participants were excluded. Finally, 640 participants were included in the analyses.

Assessments

Questionnaires consisted of the sociodemographic questionnaire, the Patient Health Questionnaire-9 (PHQ-9) for estimating depressive symptoms,[43 44] the Generalized Anxiety Disorder-7 (GAD-7) for assessing anxiety symptoms,[45 46] the Adult ADHD Self-Report Scale (ASRS-V1.1) for estimating ADHD symptoms,[47 48] and the Autism Spectrum Quotient-10 (AQ-10) for quantifying autistic traits.[49 50]

Main outcome measures

Depression symptoms were assessed by the PHQ-9.[43 44] Based directly on the nine diagnostic criteria for major depressive disorder in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV),[51] the scale consists of nine items that assess the frequency with which nine depressive symptoms had occurred in the past 2 weeks. Participants rated items as 0, 1, 2, or 3 for “not at all,” “several days,” “more than half the days,” and “nearly every day,” respectively. Responses to each item were summed to provide a

single score ranging from 0 to 27, with higher scores indicating more severe depressive symptoms.

Anxiety symptoms were assessed by the GAD-7.[45 46] The GAD-7 is derived from the 13-item criteria for GAD in the DSM-IV.[51] It consists of seven items with the highest correlation to the 13-item scale score. Participants rated the frequency of seven anxiety symptoms during the last 2 weeks as 0, 1, 2, or 3 for "not at all," "several days," "more than half the days," and "nearly every day," respectively. The responses to each item were summed to provide a single score ranging from 0 to 21, with higher scores indicating more severe anxiety symptoms.

Predictors—developmental characteristics

ADHD traits were assessed by the ASRS-V1.1 Screener.[47 48] The ASRS-V1.1 Screener was derived from the 18-item criteria for ADHD in the DSM-IV,[51] consisting of six questions considered most predictive of symptoms consistent with ADHD. The six-item questionnaire includes questions on inattention (four items) and hyperactivity symptoms (two items). Participants rated the frequency of ADHD symptoms over the past 6 months as 0, 1, 2, 3, or 4 for "never," "rarely," "sometimes," "often," and "very often," respectively. The responses to each item were summed to provide a single score ranging from 0 to 24, with higher scores indicating higher ADHD traits.

Autistic traits were assessed by the AQ-10.[49 50] The AQ-50, an original version of the AQ-10, was originally developed as a tool for screening autistic traits in intellectually able adults. Albeit a short version of the AQ-50, the AQ-10 has been well validated for measuring autistic traits.[52] Responses are rated on a four-point scale: "definitely disagree," "slightly disagree," "slightly agree," and "definitely agree." Responses indicating autistic traits were scored 1, while other responses were scored 0 (for five items, "definitely disagree" and "slightly disagree" were scored 1, but for the five reverse-scored items, "slightly agree" and "definitely agree" were scored 1). The responses to each item were summed to provide a single score ranging from 0 to 10, with higher scores indicating a higher level of autistic traits.

Predictors—changes in lifestyle

Regarding the changes in lifestyle after the COVID-19 outbreak, changes in physical and psychological burden were rated as "markedly decreased," "decreased," "unchanged," "increased," or "markedly increased" as the answers to the question "How has the physical/mental burden of work changed compared to before the COVID-19 pandemic?" Additionally, changes in income, frequency of going out, and interpersonal interactions (including online interactions) were assessed by rate of change: "Greater than or equal to 150%," "110 to 150%," "90 to 110 %," "50 to 90%," or "Less than 50%," as the answers to the question "How has your income/ frequency of going out/ interpersonal interactions (including online interactions) changed compared to before the COVID-19 pandemic?"

Other covariates

The questionnaire included items on demographic characteristics, such as age (stratified by decade), sex, body mass index (BMI), residential area (urban, suburban, or rural), number of households, smoking habit (yes/no), habitual alcohol consumption (yes/no), and history of COVID-19 infection (yes/no). Participants' work status including occupation, commuting time (< 30 min, 30 min to 1 h, or ≥ 1 h), working hours per day and number of workdays per month, engagement in night-shift (yes/no), frequency of contact with confirmed/suspected COVID-19 patients, fear of COVID-19 (no fear, moderate fear, or extreme fear), and experience of discrimination (a yes/no answer to the question, "After the COVID-19 epidemic, have you experienced discrimination in daycare centers, schools, or from community residents because you are a medical worker?") were also evaluated. In this study, we defined frontline workers as those directly involved in COVID-19 prevention and treatment and having direct contact with confirmed or suspected cases once or more than once a week.

Statistical analysis

A series of hierarchical multiple regression analyses were performed to test the effects of developmental characteristics on depression (the score of the PHQ-9) after controlling for sociodemographic

factors and changes in participants' lives after the COVID-19 outbreak. First, developmental characteristics (the ASRS score and the AQ-10 score) were entered into the regression model (Model 1). Second, changes in lifestyle after the COVID-19 outbreak (changes in physical and psychological burden, changes in income, frequency of going out, and interpersonal interaction) were entered into the regression model in the second step (Model 2). Lastly, sociodemographic variables including age group, sex, BMI, residential area, number of households, habitual smoking and alcohol consumption, history of COVID-19 infection, work status (occupation, commuting time, working hours per month, engagement in night-shifts, whether a frontline worker or not), fear of COVID-19, and experience of discrimination were entered in the third and final step (Model 3). Except for developmental characteristics, the variables used for adjustment were items that are considered to be associated with depression/anxiety in medical workers in previous studies.[2-4 8-10 12 13 15-29] The same hierarchical multiple regression analyses were performed to test the effects of developmental characteristics on anxiety (GAD-7 score). We used SPSS statistics version 22 (SPSS Japan, Inc., Tokyo Japan) to perform all analyses. Statistical significance was set at $p<0.05$.

Patient and public involvement

There was no patient or public involvement in the production of this study.

RESULTS

The 640 participants consisted of 270 (42.2%) physicians (including dentists), 190 (29.7%) nurses (including midwives), and 180 (28.1%) other workers (pharmacists (n=34), nutritionists (n=4), radiologists (n=4), clinical technologists (n=17), physical therapists (n=6), occupational therapists (n=14), certified orthoptists (n=1), clinical engineers (n=4), speech therapists (n=8), certified care workers (n=3), clinical psychologists (n=25), psychiatric social workers (n=13), music therapists (n=1), medical assistants (n=7), and office workers (n=39)). Most of the participants worked in hospitals (n=516), followed by outpatient clinics (n=88), and other medical institutions including pharmacies, long-term care facilities, and public health

centers (n=36). The respondents were aged between 20 to 70 (one respondent was in his 70s but was included in the '≥60' category in the analysis), with the majority in their 30s and 40s (37.3% and 34.8%, respectively), and 359 (59.1%) were female. Only five participants (0.8%) had a history of COVID-19 infection. Forty-six participants (7.2%) were frontline workers. Other descriptive information of the participants is presented in Table 1. A majority of the participants (85.4%) were concerned about COVID-19, and about 20% of them were extremely fearful of COVID-19 (17.7% of all participants). Discrimination against medical workers was experienced by 8.8% of the respondents. The prevalence of clinically significant depressive symptoms (PHQ-9≥10), anxiety symptoms (GAD-7≥10), ADHD traits (ASRS≥14) and autistic traits (AQ-10≥6) were 77 (12.0%), 54 (8.4%), 65 (10.2%), and 64 (10.0%), respectively.

Table 1. Demographic data and employment status of participants (n=640)

Age group (years), N (%)	
20 to 29	75 (11.7)
30 to 39	239 (37.3)
40 to 49	223 (34.8)
50 to 59	74 (11.6)
≥60	29 (4.5)
Female, N (%)	359 (56.1)
Body mass index, median (IQR), kg/m2	21.8 (20.1–24.2)
Residential area, N (%)	
Urban	260 (40.6)
Suburban	279 (43.6)
Rural	101 (15.8)
Number of households, N (%)	
1	187 (29.7)
2	139 (21.7)
3	130 (20.3)
≥4	184 (28.7)
Habitual smoking, N (%)	60 (9.4)
Habitual alcohol consumption, N (%)	170 (26.6)
COVID-19 infection, N (%)	5 (0.8)
Occupation, N (%)	
Physician	270 (42.2)
Nurse	190 (29.7)
Other worker	180 (28.1)
Commuting time, N (%)	
<30 min	374 (58.4)
30 min to 1 h	183 (28.6)
≥1 h	83 (13.0)
Working hours, median (IQR), per month	207.5 (187–247)
Working night-shift, N (%)	316 (49.4)
Frontline worker, N (%)	46 (7.2)

Fear of COVID-19, N (%)	
No fear	94 (14.7)
Moderate fear	433 (67.7)
Extreme fear	113 (17.7)
Experience of discrimination, N (%)	56 (8.8)
PHQ-9 score, median (IQR), points	4 (1–8)
GAD-7 score, median (IQR), points	2 (0–5)
ASRS score, median (IQR), points	9 (6–11)
AQ-10 score, median (IQR), points	3 (2–4)

IQR, interquartile rage; PHQ-9, Patient Health Questionnaire-9; GAD-7, Generalized Anxiety Disorder-7; ASRS, Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale; AQ-10, Autism-Spectrum Quotient-10.

Changes in lifestyle (physical and psychological burden, income, frequency of going out, and interpersonal interaction) are shown in Figure 2. In terms of workload after the COVID-19 outbreak, 49.1% and 78.3% of the participants reported that their physical and psychological burdens increased, respectively. As for income, only 19.7% of the subjects experienced a decrease below 90%. Overall, a noticeable decrease in the frequency of going out was reported—92.2% reported reducing activities by 10% or more, and 40% reported reducing their activities by 50% or more. A similar decrease in interpersonal interaction was noted, with 83.5% reporting a decrease of less than 90% and 37.7% reporting a decrease of less than 50%.

To evaluate the effect of developmental characteristics, changes in lifestyle due to COVID-19, and sociodemographic variables, we performed two separate regression analyses. For depression, the first model testing the contributions of developmental characteristics were statistically significant (R^2=21.7%, $p<0.001$). The addition of changes in lifestyle due to COVID-19 (Model 2) resulted in a significant increase in the R^2 value (ΔR^2=12.6%, $p<0.001$). The final model (the standard multiple regression analysis) in which all of the variables were entered simultaneously explained 43.3% of the variance in depression. Finally, ASRS score (β=0.390, $p<0.001$), AQ-10 score (β=0.069, $p<0.05$), changes in physical burden (β=0.121, $p<0.01$), changes in psychological burden (β=0.161, $p<0.001$), changes in interpersonal interaction (β=0.103, $p<0.01$), being female (β=0.199, $p<0.001$), body mass index (β=0.094, $p<0.01$), number of households (β=−0.086, $p<0.01$), habitual smoking (β=0.068, $p<0.05$), other worker (β=0.130, $p<0.001$), working hours per month (β=0.083, $p<0.05$), fear of COVID-19 (β=0.135, $p<0.001$), and experience of discrimination (β=0.069, $p<0.05$) were

identified as significant correlates of depression. However, the correlation between AQ-10 score and depression was not significant in the bivariate analysis (Table 2).

Table 2. Multiple linear regression model predicting depressive symptoms*

Predictors	Model 1			Model 2			Model 3		
	B	*SE*	*β*	*B*	*SE*	*β*	*B*	*SE*	*β*
Step 1: Developmental characteristics									
ASRS score (continuous variable)	0.562	0.043	0.463‖‖	0.508	0.04	0.418‖‖	0.474	0.039	0.390‖‖
AQ-10 score (continuous variable)	0.045	0.096	0.017	0.113	0.089	0.042	0.186	0.086	0.069‡‡
Step 2: Changes in lifestyle after the COVID-19 outbreak									
Changes in physical burden†				0.745	0.190	0.151‖‖	0.595	0.184	0.121§§
Changes in psychological burden†				1.315	0.244	0.216‖‖	0.978	0.243	0.161‖‖
Changes in income‡				−0.124	0.319	−0.013	−0.196	0.313	−0.020
Changes in frequency of going out‡				−0.324	0.277	−0.042	−0.515	0.264	−0.066
Changes in interpersonal interaction‡				0.791	0.226	0.124‖‖	0.657	0.216	0.103§§
Step 3: Sociodemographic variables									
Age group§							−0.045	0.159	−0.009
Female (yes)							1.937	0.358	0.199‖‖
Body mass index (continuous variable)							0.134	0.047	0.094§§
Residential area‖							−0.223	0.230	−0.033
Number of households¶							−0.349	0.132	−0.086§§
Habitual smoking (yes)							1.137	0.526	0.068‡‡
Habitual alcohol consumption (yes)							0.448	0.348	0.041
History of COVID-19 infection (yes)							2.021	1.693	0.037
Occupation									
Physician (reference)							—		—
Nurse							−0.131	0.425	−0.012
Other worker							1.399	0.423	0.130‖‖
Commuting time**							−0.067	0.217	−0.010
Working hours per month (continuous variable)							0.008	0.003	0.083‡‡
Working night shift (yes)							−0.099	0.343	−0.010
Frontline worker (yes)							0.233	0.602	0.012
Fear of COVID-19††							1.151	0.278	0.135‖‖
Experience of discrimination (yes)							1.176	0.548	0.069‡‡
Fit test									
R^2			0.217			0.342			0.433
Change in R^2			0.217			0.126			0.091

SE, standard error; ASRS, the Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale; AQ-10, the Autism-Spectrum Quotient-10.
*Evaluated using the Patient Health Questionnaire-9.
†markedly decreased=1, decreased=2, not changed=3, increased=4, and markedly increased=5.
‡≥150=1, 110 to 15%=2, 90 to 110%=3, 50 to 90%=4, and <50%=5.
§20 to 29=1, 30 to 39=2, 40 to 49=3, 50 to 59=4, and 60 or over 60=5.
‖urban=1, suburban=2, rural=3.
¶4 or more than 4 was calculated as '4'.
**<30 min=1, 30 min to 1 h=2, ≥1 h=3.
††No fear=1, moderate fear=2, extreme fear=3.
‡‡p<0.05, §§p<0.01, ‖‖p<0.001.

For anxiety, the first model testing the contributions of developmental characteristics were statistically significant (R^2=22.5%, p<0.001). The addition of changes in lifestyle with COVID-19 (model 2) resulted in a significant increase in the R^2 value (ΔR^2=0.105%, p<0.001). The final full model (the standard

multiple regression analysis) in which all of the variables were entered simultaneously explained 39% of the variance in anxiety. Finally, the ASRS score (β=0.426, p<0.001), changes in physical burden (β=0.120, p<0.01), changes in psychological burden (β=0.146, p<0.001), being female (β=0.089, p<0.05), other worker (β=0.123, p<0.001), fear of COVID-19 (β=0.170, p<0.001), and experience of discrimination (β=0.067, p<0.05) were identified as significant correlates of anxiety (Table 3).

Table 3. Multiple linear regression model predicting anxiety symptoms*

Predictors	Model 1			Model 2			Model 3		
	B	*SE*	*β*	*B*	*SE*	*β*	*B*	*SE*	*β*
Step 1: Developmental characteristics									
ASRS score (continuous variable)	0.480	0.036	0.472‖‖	0.438	0.034	0.431‖‖	0.433	0.033	0.426‖‖
AQ-10 score (continuous variable)	0.029	0.080	0.013	0.079	0.075	0.035	0.117	0.075	0.052
Step 2: Changes in lifestyle after the COVID-19 outbreak									
Changes in physical burden†				0.643	0.160	0.156‖‖	0.492	0.159	0.120§§
Changes in psychological burden†				0.969	0.206	0.191‖‖	0.743	0.211	0.146‖‖
Changes in income‡				0.007	0.269	0.001	−0.116	0.272	−0.014
Changes in frequency of going out‡				−0.223	0.233	−0.034	−0.257	0.229	−0.040
Changes in interpersonal interaction‡				0.507	0.190	0.095§§	0.367	0.188	0.069
Step 3: Sociodemographic variables									
Age group§							0.212	0.138	0.052
Female (yes)							0.727	0.310	0.089‡‡
Body mass index (continuous variable)							−0.015	0.040	−0.013
Residential area‖							−0.061	0.200	−0.011
Number of households¶							−0.066	0.114	−0.019
Habitual smoking (yes)							0.336	0.456	0.024
Habitual alcohol consumption (yes)							0.244	0.302	0.027
History of COVID-19 infection (yes)							1.870	1.469	0.041
Occupation									
Physician (reference)							—		—
Nurse							−0.031	0.369	−0.004
Other worker							1.108	0.367	0.123§§
Commuting time**							−0.169	0.188	−0.030
Working hours per month (continuous variable)							0.001	0.003	0.015
Working night shift (yes)							0.071	0.298	0.009
Frontline worker (yes)							0.434	0.522	0.028
Fear of COVID-19††							1.214	0.241	0.170‖‖
Experience of discrimination (yes)							0.956	0.475	0.067‡‡
Fit test									
R^2			0.225			0.330			0.390
Change in R^2			0.225			0.105			0.060

SE, standard error; ASRS, the Adult Attention-Deficit/Hyperactivity Disorder Self-Report Scale; AQ-10, the Autism-Spectrum Quotient-10.
*Evaluated using the Generalized Anxiety Disorder-7.
†markedly decreased=1, decreased=2, not changed=3, increased=4, and markedly increased=5.
‡≥150=1, 110 to 15%=2, 90 to 110%=3, 50 to 90%=4, and <50%=5.
§20 to 29=1, 30 to 39=2, 40 to 49=3, 50 to 59=4, and 60 or over 60=5.
‖urban=1, suburban=2, rural=3.
¶4 or more than 4 was calculated as '4'.
**<30 min=1, 30 min to 1 h=2, ≥1 h=3.
††No fear=1, moderate fear=2, extreme fear=3.
‡‡p<0.05, §§p<0.01, ‖‖p<0.001.

DISCUSSION

This study was conducted during the COVID-19 outbreak, but is the first study investigating the influence of developmental characteristics on depression and anxiety in medical workers. Results indicated that ADHD traits might have a strong influence on depression and anxiety symptoms even after controlling for physical and psychological burden and fear of COVID-19, with its effect possibly being greater than other factors, including autistic traits.

In general, and not only during a pandemic, the relationship between ADHD and depression or anxiety has already been addressed.[53-58] Additionally, ASD patients in general are more prone to developing depression and anxiety.[16] However, in this study, wherein a strong correlation was found between ADHD traits and depression/anxiety symptoms, there was no significant correlation for autistic traits. The difference in the association between the two traits for depression/anxiety is not clear. One possible reason for the strong correlation between ADHD traits and depression/anxiety is that people with ADHD traits may have faced a higher risk of infection due to their own inattention and impulsivity, which can be an obvious stressor among medical workers. Even though untreated ADHD is a risk factor for acquiring COVID-19,[40 41] the relationship between ADHD traits and compliance with infection control measures under the pandemic remains unclear and should be examined in the future. Further, due to the calls for self-restraint by government leaders,[31] those with high ADHD traits may have experienced high stress;[59] self-restraint prevents one from engaging in a variety of activities, and it would be difficult for people with ADHD traits to adapt to such activities even after months or years. Meanwhile, against the intolerance of change in ASD,[42] people with autistic traits may have shown some level of adaption to the situation, as the survey was conducted more than 6 months after the COVID-19 outbreak. Furthermore, unnecessary outings or interpersonal interactions, which can be stressors for people with autistic traits,[60] have been reduced due to COVID-19. It is also noteworthy that the correlation between autistic traits and depression, which was not significant in the bivariate analysis, was significant in the multivariate analysis. This makes it undeniable that autistic traits are also a unique factor that can be

associated with depression. As there have been no studies that examined developmental characteristics and their psychological effects in the general adult population, it can be inferred that the relationship between psychological burden and ADHD or autistic traits after the COVID-19 outbreak should be evaluated and further investigated not only among health care workers but also among the general population. Contrary to the above hypothesis that reducing unnecessary interpersonal interaction could be protective for individuals with autistic traits, this study highlighted the importance of maintaining interpersonal interactions to fight depression. Both belonging to a large household and maintaining interpersonal interactions had a protective effect against depression symptoms. This result is consistent with the known importance of receiving direct social support from friends, family, colleagues, and supervisors during a pandemic, which has already been suggested in numerous studies.[3 4 8-10 12] In this study, the association between changes in interpersonal interaction and anxiety symptoms was not significant; this may be because reduced interpersonal interaction may lower the risk of infection and could thus reduce anxiety. Contrarily, the experience of discriminatory treatment was independently associated with both depression and anxiety symptoms. The negative psychological impact of discrimination on health care workers has been reported in previous pandemics, such as severe acute respiratory syndrome, Middle East respiratory syndrome, or other viral infections.[3 4] This study's results are consistent with the findings of the COVID-19 outbreak, which also revealed the incidence of mental disorders due to discrimination. [22-25]

Factors related to employment can also be a psychological burden for medical workers. Several studies have shown that the psychological burden on health care workers is high not only in countries severely affected by the pandemic but also in relatively unaffected countries.[17 18 21 29] We found that the physical and psychological burden of the COVID-19 outbreak was increased in around 50% and 80% of medical workers, respectively. Both increases in psychological and physical burden were independently associated with symptoms of depression and anxiety, which is consistent with previous studies.[19 20] It has also been reported that protective garments can increase physical burden[61 62] and that strict infection control measures can increase stress levels.[19] In addition to changes in physical and psychological burden, long working hours were significantly correlated with depression symptoms in this study. This was consistent with some studies on the

association between long working hours and depression or increased stress under the COVID-19 outbreak.[27 28] Furthermore, a significant association between the fear of COVID-19, depression, and anxiety has been replicated, which is consistent with previous study findings.[2 4 10] Despite the increased psychological and physical burden and fear of COVID-19, the prevalence of clinically significant symptoms of depression and anxiety was lower than among health care workers in other nations.[7 9 13 14 17] This may reflect the low number of dominant COVID-19 patients and the low number of deaths due to COVID-19 in Japan as compared to other countries.[30] In addition, the low prevalence of clinically significant symptoms of depression and anxiety could be attributed to the current study's small sample of medical workers who had direct contact with COVID-19 patients compared to the sample size in previously conducted studies.[11-13 63 64] Besides, unlike previous reports on the general population,[65-68] the association between the income loss associated with the COVID-19 outbreak, depression, and anxiety was not clear in this study. This can be due to the limited number of medical workers who experienced a decline in income; the impact could be greater if the economy had collapsed, and their incomes had drastically decreased.

The current results suggested that, remarkably, medical workers other than physicians or nurses have an independent risk of both depression and anxiety. In terms of occupation, although frontline physicians had a higher incidence of depression than other occupations,[14] numerous studies on health care workers have reported lower depression and anxiety in physicians than in other occupations,[3 4 7-9 13 21 26] as in this study. For health care workers other than physicians and nurses, one study reported that anxiety was significantly higher, but depression was comparable.[69] Another study conducted on a cruise ship during the early stages of the COVID-19 epidemic in Japan reported that distress was significantly stronger among clerical workers than physicians or nurses,[70] which are consistent with the results of the current study. Even in health care workers, inadequate medical knowledge was reported to be associated with increased levels of anxiety and depression.[3 71 72] Moreover, numerous reports have stated that fewer years of health care experience was associated with worse mental health outcomes;[3 7] other medical workers in this study may have had less experience in infection prevention. Therefore, both job-specific support and appropriate knowledge development would be important to improve the psychological burden of medical workers.

In terms of demographic variables, being female, BMI, and smoking habits were independently associated with depression symptoms. Being female was also independently associated with anxiety symptoms. The association between age and depression/anxiety was not noticeable in this study; it is still controversial in previous reports examining the association between age and psychological burden in health care workers under the pandemic.[5 9 12 17 18 21 26 27] The association between BMI, smoking habits, and depression has long been shown in the general population[73 74] and may not be unique to the COVID-19 outbreak. The association of sex, especially being a woman with depression and anxiety, has been reported in a number of studies conducted on health care workers after the onset of the COVID-19 pandemic.[2-4 8 12 13 15-17 21 26] This may also reflect the higher prevalence of depression and anxiety among women in the general population;[75 76] however, these relationships can be unique to the COVID-19 pandemic. Experimental studies have shown that women are more responsive to neural networks associated with fear and arousal responses than men;[77] the response to fear associated with COVID-19 may have been stronger in women than men. In addition, there are indications that the sociological burden on women has increased after the COVID-19 outbreak.[78] Moreover, a longitudinal study of women with children showed that depression and anxiety were higher among women who had disrupted income, difficulty balancing work and family education, and difficulty obtaining daycare.[79] Indeed, in Japan, it has been reported that suicide among women increased significantly after the COVID-19 outbreak.[80] The direct causes of depression and anxiety in females, and what interventions are best for them should be examined in the future.

There are some limitations to this study. First, the present study adopted the snowball sampling strategy with online recruitment, and thus did not specify how the questionnaire was disseminated. While this approach is valuable for exploratory studies and provides access to the target population and is used in some epidemiological studies to examine the psychological burden of health care workers under the COVID-19 outbreak,[26 27 71 72] it can still hinder the generalizability of the results as the representativeness of the sample is not guaranteed. In particular, the reliability of the prevalence rate remains problematic. Second, the participants with ADHD or autistic traits in this study were not formally diagnosed as having ADHD or ASD. In addition, determining whether they are traits or symptoms can be difficult using the questionnaire method.

The possibility that ADHD and autistic symptoms can change with age[81] is also a limitation of this study. Third, the clinically significant depressive and anxiety symptoms in this study were not those of formally diagnosed major depressive disorder or generalized anxiety disorder, respectively. Furthermore, the ASRS-V1.1, AQ-10, PHQ-9, and GAD-7 used in this study are all based on the DSM-IV diagnostic criteria and not on the latest DSM-5[82]. Fourth, the questionnaire did not include whether the respondents were receiving treatment for mental or physical illnesses, so the influence of comorbidities could not be verified in this study. Fifth, the study only examined the changes in income, frequency of going out, and interpersonal interaction, and did not assess baseline status. In particular, we did not investigate economic status, which is thought to strongly influence depression and anxiety. As this study included people working in medical institutions, it may have been biased toward middle- and high-income populations in Japan. Lastly, owing to the observational nature of the study, our findings did not show a direct causal relationship between developmental characteristics and psychological burden. In addition, as this study was conducted anonymously, it is not possible to conduct further longitudinal studies using the same participants.

The present study suggested that individual developmental characteristics, especially ADHD traits, have a considerable effect on the psychological health of medical workers. In contrast, the relationship between autistic traits and depression/anxiety symptoms was less significant. Identifying the stressors in medical workers with high ADHD traits and the subsequent development of appropriate interventions for them are warranted. Furthermore, as this was a cross-sectional study, causality cannot be determined. To verify the relationship between specific developmental characteristics and stress-related outcomes, further prospective studies with both health care workers and the general population should be conducted.

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Contributors

KM, RO, NA, and MH had full access to all of the data and took responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: KM, TY, AT, KN, TU, KY, and KK. Acquisition, analysis or interpretation of data: all authors. Drafting of the manuscript: KM. Critical revision of the manuscript for important intellectual content: all authors. Statistical analysis: KM. Obtained funding: KM. Supervision: TY, MF, KK. All authors have contributed significantly to this work and have met the qualification of authorship.

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Competing interests

None declared.

Ethics approval

The study protocol was approved by the ethical committee of the National Center of Neurology and Psychiatry (A2020-044). All subjects provided their informed consent electronically prior to the enrollment. On the informed consent page, dichotomic option was presented: yes or no. Only subjects who selected "yes" were directed to the questionnaire page, and subjects could terminate their participation at any time. The data collected did not contain any personal information.

Data availability statement

The data that support the findings of this study are available from the corresponding author on reasonable request.

REFERENCES

1. Chew QH, Wei KC, Vasoo S, et al. Psychological and Coping Responses of Health Care Workers Toward Emerging Infectious Disease Outbreaks: A Rapid Review and Practical Implications for the COVID-19 Pandemic. *The Journal of clinical psychiatry* 2020;81(6) doi: 10.4088/JCP.20r13450 [published Online First: 2020/10/22]
2. Serrano-Ripoll MJ, Meneses-Echavez JF, Ricci-Cabello I, et al. Impact of viral epidemic outbreaks on mental health of healthcare workers: a rapid systematic review and meta-analysis. *Journal of affective disorders* 2020;277:347-57. doi: 10.1016/j.jad.2020.08.034 [published Online First: 2020/08/31]
3. Sirois FM, Owens J. Factors Associated With Psychological Distress in Health-Care Workers During an Infectious Disease Outbreak: A Rapid Systematic Review of the Evidence. *Frontiers in psychiatry* 2020;11:589545. doi: 10.3389/fpsyt.2020.589545 [published Online First: 2021/02/16]
4. Cabarkapa S, Nadjidai SE, Murgier J, et al. The psychological impact of COVID-19 and other viral epidemics on frontline healthcare workers and ways to address it: A rapid systematic review. *Brain, behavior, & immunity - health* 2020;8:100144. doi: 10.1016/j.bbih.2020.100144 [published Online First: 2020/09/23]
5. Kisely S, Warren N, McMahon L, et al. Occurrence, prevention, and management of the psychological effects of emerging virus outbreaks on healthcare workers: rapid review and meta-analysis. *Bmj* 2020;369:m1642. doi: 10.1136/bmj.m1642 [published Online First: 2020/05/07]
6. Xiang YT, Yang Y, Li W, et al. Timely mental health care for the 2019 novel coronavirus outbreak is urgently needed. *Lancet Psychiatry* 2020;7(3):228-29. doi: 10.1016/s2215-0366(20)30046-8 [published Online First: 2020/02/08]
7. Sanghera J, Pattani N, Hashmi Y, et al. The impact of SARS-CoV-2 on the mental health of healthcare workers in a hospital setting-A Systematic Review. *Journal of occupational health* 2020;62(1):e12175. doi: 10.1002/1348-9585.12175 [published Online First: 2020/11/02]
8. Pappa S, Ntella V, Giannakas T, et al. Prevalence of depression, anxiety, and insomnia among healthcare workers during the COVID-19 pandemic: A systematic review and meta-analysis. *Brain, behavior, and immunity* 2020;88:901-07. doi: 10.1016/j.bbi.2020.05.026 [published Online First: 2020/05/22]
9. Luo M, Guo L, Yu M, et al. The psychological and mental impact of coronavirus disease 2019 (COVID-19) on medical staff and general public - A systematic review and meta-analysis. *Psychiatry research* 2020;291:113190. doi: 10.1016/j.psychres.2020.113190 [published Online First: 2020/06/22]
10. Muller AE, Hafstad EV, Himmels JPW, et al. The mental health impact of the covid-19 pandemic on healthcare workers, and interventions to help them: A rapid systematic review. *Psychiatry research* 2020;293:113441. doi: 10.1016/j.psychres.2020.113441 [published Online First: 2020/09/09]
11. da Silva FCT, Neto MLR. Psychiatric symptomatology associated with depression, anxiety, distress, and insomnia in health professionals working in patients affected by COVID-19: A systematic review with meta-analysis. *Progress in neuro-psychopharmacology & biological psychiatry* 2021;104:110057. doi: 10.1016/j.pnpbp.2020.110057 [published Online First: 2020/08/11]
12. Vindegaard N, Benros ME. COVID-19 pandemic and mental health consequences: Systematic review of the current evidence. *Brain, behavior, and immunity* 2020;89:531-42. doi: 10.1016/j.bbi.2020.05.048 [published

Online First: 2020/06/03]

13. Vizheh M, Qorbani M, Arzaghi SM, et al. The mental health of healthcare workers in the COVID-19 pandemic: A systematic review. *Journal of diabetes and metabolic disorders* 2020:1-12. doi: 10.1007/s40200-020-00643-9 [published Online First: 2020/11/03]
14. Salari N, Khazaie H, Hosseinian-Far A, et al. The prevalence of stress, anxiety and depression within front-line healthcare workers caring for COVID-19 patients: a systematic review and meta-regression. *Human resources for health* 2020;18(1):100. doi: 10.1186/s12960-020-00544-1 [published Online First: 2020/12/19]
15. Mutluer T, Doenyas C, Aslan Genc H. Behavioral Implications of the Covid-19 Process for Autism Spectrum Disorder, and Individuals' Comprehension of and Reactions to the Pandemic Conditions. *Frontiers in psychiatry* 2020;11:561882. doi: 10.3389/fpsyt.2020.561882 [published Online First: 2020/12/12]
16. Hollocks MJ, Lerh JW, Magiati I, et al. Anxiety and depression in adults with autism spectrum disorder: a systematic review and meta-analysis. *Psychological medicine* 2019;49(4):559-72. doi: 10.1017/s0033291718002283 [published Online First: 2018/09/05]
17. Nayak BS, Sahu PK, Ramsaroop K, et al. Prevalence and factors associated with depression, anxiety and stress among healthcare workers of Trinidad and Tobago during COVID-19 pandemic: a cross-sectional study. *BMJ open* 2021;11(4):e044397. doi: 10.1136/bmjopen-2020-044397 [published Online First: 2021/04/15]
18. Tran TV, Nguyen HC, Pham LV, et al. Impacts and interactions of COVID-19 response involvement, health-related behaviours, health literacy on anxiety, depression and health-related quality of life among healthcare workers: a cross-sectional study. *BMJ open* 2020;10(12):e041394. doi: 10.1136/bmjopen-2020-041394 [published Online First: 2020/12/10]
19. Zhang C, Yang L, Liu S, et al. Survey of Insomnia and Related Social Psychological Factors Among Medical Staff Involved in the 2019 Novel Coronavirus Disease Outbreak. *Frontiers in psychiatry* 2020;11:306. doi: 10.3389/fpsyt.2020.00306 [published Online First: 2020/04/30]
20. Du J, Dong L, Wang T, et al. Psychological symptoms among frontline healthcare workers during COVID-19 outbreak in Wuhan. *General hospital psychiatry* 2020;67:144-45. doi: 10.1016/j.genhosppsych.2020.03.011 [published Online First: 2020/05/10]
21. Chatzittofis A, Karanikola M, Michailidou K, et al. Impact of the COVID-19 Pandemic on the Mental Health of Healthcare Workers. *International journal of environmental research and public health* 2021;18(4) doi: 10.3390/ijerph18041435 [published Online First: 2021/02/07]
22. Rana W, Mukhtar S, Mukhtar S. Mental health of medical workers in Pakistan during the pandemic COVID-19 outbreak. *Asian journal of psychiatry* 2020;51:102080. doi: 10.1016/j.ajp.2020.102080 [published Online First: 2020/04/14]
23. Singh R, Subedi M. COVID-19 and stigma: Social discrimination towards frontline healthcare providers and COVID-19 recovered patients in Nepal. *Asian journal of psychiatry* 2020;53:102222-22. doi: 10.1016/j.ajp.2020.102222 [published Online First: 2020/06/13]
24. Abdel Wahed WY, Hefzy EM, Ahmed MI, et al. Assessment of Knowledge, Attitudes, and Perception of Health Care Workers Regarding COVID-19, A Cross-Sectional Study from Egypt. *J Community Health* 2020;45(6):1242-51. doi: 10.1007/s10900-020-00882-0
25. Chatterjee SS, Bhattacharyya R, Bhattacharyya S, et al. Attitude, practice, behavior, and mental health impact

of COVID-19 on doctors. *Indian J Psychiatry* 2020;62(3):257-65. doi: 10.4103/psychiatry.IndianJPsychiatry_333_20 [published Online First: 2020/08/11]

26. Rossi R, Socci V, Pacitti F, et al. Mental Health Outcomes Among Frontline and Second-Line Health Care Workers During the Coronavirus Disease 2019 (COVID-19) Pandemic in Italy. *JAMA network open* 2020;3(5):e2010185. doi: 10.1001/jamanetworkopen.2020.10185 [published Online First: 2020/05/29]
27. Song X, Fu W, Liu X, et al. Mental health status of medical staff in emergency departments during the Coronavirus disease 2019 epidemic in China. *Brain, behavior, and immunity* 2020;88:60-65. doi: 10.1016/j.bbi.2020.06.002 [published Online First: 2020/06/09]
28. Mo Y, Deng L, Zhang L, et al. Work stress among Chinese nurses to support Wuhan in fighting against COVID-19 epidemic. *Journal of nursing management* 2020;28(5):1002-09. doi: 10.1111/jonm.13014 [published Online First: 2020/04/08]
29. Lu MY, Ahorsu DK, Kukreti S, et al. The Prevalence of Post-traumatic Stress Disorder Symptoms, Sleep Problems, and Psychological Distress Among COVID-19 Frontline Healthcare Workers in Taiwan. *Frontiers in psychiatry* 2021;12:705657. doi: 10.3389/fpsyt.2021.705657 [published Online First: 2021/07/30]
30. Johns Hopkins University. COVID-19 Dashboard by the Center for Systems Science and Engineering (CSSE). Available from: https:coronavirus.jhu.edu/map.htmlhttps:coronavirus.jhu.edu/map.html. [Accessed 15 Feb 2021].
31. Tokumoto A, Akaba H, Oshitani H, et al. COVID-19 Health system response monitor: Japan. New Delhi: World Health Organization. Regional Office for South-East Asia 2020.
32. Furuse Y, Sando E, Tsuchiya N, et al. Clusters of Coronavirus Disease in Communities, Japan, January-April 2020. *Emerging infectious diseases* 2020;26(9):2176-9. doi: 10.3201/eid2609.202272 [published Online First: 2020/06/11]
33. Rotenstein LS, Torre M, Ramos MA, et al. Prevalence of Burnout Among Physicians: A Systematic Review. *Jama* 2018;320(11):1131-50. doi: 10.1001/jama.2018.12777 [published Online First: 2018/10/17]
34. Colizzi M, Sironi E, Antonini F, et al. Psychosocial and Behavioral Impact of COVID-19 in Autism Spectrum Disorder: An Online Parent Survey. *Brain sciences* 2020;10(6) doi: 10.3390/brainsci10060341 [published Online First: 2020/06/07]
35. Melegari MG, Giallonardo M, Sacco R, et al. Identifying the impact of the confinement of Covid-19 on emotional-mood and behavioural dimensions in children and adolescents with attention deficit hyperactivity disorder (ADHD). *Psychiatry research* 2020;296:113692. doi: 10.1016/j.psychres.2020.113692 [published Online First: 2021/01/10]
36. Bobo E, Lin L, Acquaviva E, et al. [How do children and adolescents with Attention Deficit Hyperactivity Disorder (ADHD) experience lockdown during the COVID-19 outbreak?]. *L'Encephale* 2020;46(3s):S85-s92. doi: 10.1016/j.encep.2020.05.011 [published Online First: 2020/06/12]
37. Sciberras E, Patel P, Stokes MA, et al. Physical Health, Media Use, and Mental Health in Children and Adolescents With ADHD During the COVID-19 Pandemic in Australia. *Journal of attention disorders* 2020:1087054720978549. doi: 10.1177/1087054720978549 [published Online First: 2020/12/18]
38. Amorim R, Catarino S, Miragaia P, et al. The impact of COVID-19 on children with autism spectrum disorder.

Revista de neurologia 2020;71(8):285-91. doi: 10.33588/rn.7108.2020381 [published Online First: 2020/10/10]

39. Antshel KM, Russo N. Autism Spectrum Disorders and ADHD: Overlapping Phenomenology, Diagnostic Issues, and Treatment Considerations. *Current psychiatry reports* 2019;21(5):34. doi: 10.1007/s11920-019-1020-5 [published Online First: 2019/03/25]
40. Merzon E, Manor I, Rotem A, et al. ADHD as a Risk Factor for Infection With Covid-19. *Journal of attention disorders* 2020:1087054720943271. doi: 10.1177/1087054720943271 [published Online First: 2020/07/23]
41. Wang Q, Xu R, Volkow ND. Increased risk of COVID-19 infection and mortality in people with mental disorders: analysis from electronic health records in the United States. *World psychiatry : official journal of the World Psychiatric Association (WPA)* 2021;20(1):124-30. doi: 10.1002/wps.20806 [published Online First: 2020/10/08]
42. Lawson RP, Mathys C, Rees G. Adults with autism overestimate the volatility of the sensory environment. *Nature neuroscience* 2017;20(9):1293-99. doi: 10.1038/nn.4615 [published Online First: 2017/08/02]
43. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *Journal of general internal medicine* 2001;16(9):606-13. doi: 10.1046/j.1525-1497.2001.016009606.x [published Online First: 2001/09/15]
44. Muramatsu K, Miyaoka H, Kamijima K, et al. Performance of the Japanese version of the Patient Health Questionnaire-9 (J-PHQ-9) for depression in primary care. *General hospital psychiatry* 2018;52:64-69. doi: 10.1016/j.genhosppsych.2018.03.007 [published Online First: 2018/04/27]
45. Spitzer RL, Kroenke K, Williams JB, et al. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med* 2006;166(10):1092-7. doi: 10.1001/archinte.166.10.1092 [published Online First: 2006/05/24]
46. Validation and utility of a Japanese version of the GAD-7 2009.
47. Kessler RC, Adler L, Ames M, et al. The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. *Psychological medicine* 2005;35(2):245-56. doi: 10.1017/s0033291704002892 [published Online First: 2005/04/22]
48. Kessler RC, Adler LA, Gruber MJ, et al. Validity of the World Health Organization Adult ADHD Self-Report Scale (ASRS) Screener in a representative sample of health plan members. *International journal of methods in psychiatric research* 2007;16(2):52-65. doi: 10.1002/mpr.208 [published Online First: 2007/07/12]
49. Baron-Cohen S, Wheelwright S, Skinner R, et al. The autism-spectrum quotient (AQ): evidence from Asperger syndrome/high-functioning autism, males and females, scientists and mathematicians. *Journal of autism and developmental disorders* 2001;31(1):5-17. doi: 10.1023/a:1005653411471 [published Online First: 2001/07/07]
50. Kurita H, Koyama T, Osada H. Autism-Spectrum Quotient-Japanese version and its short forms for screening normally intelligent persons with pervasive developmental disorders. *Psychiatry and clinical neurosciences* 2005;59(4):490-6. doi: 10.1111/j.1440-1819.2005.01403.x [published Online First: 2005/07/29]
51. American Psychiatric Association. DSM-IV: Diagnostic and statistical manual (Fourth Edition). Washington,

DC: American Psychiatric Association 1994.

52. Lundin A, Kosidou K, Dalman C. Measuring Autism Traits in the Adult General Population with the Brief Autism-Spectrum Quotient, AQ-10: Findings from the Stockholm Public Health Cohort. *Journal of autism and developmental disorders* 2019;49(2):773-80. doi: 10.1007/s10803-018-3749-9 [published Online First: 2018/09/24]
53. Nankoo MMA, Palermo R, Bell JA, et al. Examining the Rate of Self-Reported ADHD-Related Traits and Endorsement of Depression, Anxiety, Stress, and Autistic-Like Traits in Australian University Students. *Journal of attention disorders* 2019;23(8):869-86. doi: 10.1177/1087054718758901 [published Online First: 2018/03/06]
54. Combs MA, Canu WH, Broman-Fulks JJ, et al. Perceived stress and ADHD symptoms in adults. *Journal of attention disorders* 2015;19(5):425-34. doi: 10.1177/1087054712459558 [published Online First: 2012/10/05]
55. Evren B, Evren C, Dalbudak E, et al. The impact of depression, anxiety, neuroticism, and severity of Internet addiction symptoms on the relationship between probable ADHD and severity of insomnia among young adults. *Psychiatry research* 2019;271:726-31. doi: 10.1016/j.psychres.2018.12.010 [published Online First: 2019/02/23]
56. Shen Y, Zhang Y, Chan BSM, et al. Association of ADHD symptoms, depression and suicidal behaviors with anxiety in Chinese medical college students. *BMC Psychiatry* 2020;20(1):180. doi: 10.1186/s12888-020-02555-7 [published Online First: 2020/04/24]
57. Mohamed SMH, Börger NA, van der Meere JJ. Executive and Daily Life Functioning Influence the Relationship Between ADHD and Mood Symptoms in University Students. *Journal of attention disorders* 2020:1087054719900251. doi: 10.1177/1087054719900251 [published Online First: 2020/01/24]
58. Oh Y, Yoon HJ, Kim JH, et al. Trait Anxiety as a Mediator of the Association between Attention Deficit Hyperactivity Disorder Symptom Severity and Functional Impairment. *Clinical psychopharmacology and neuroscience : the official scientific journal of the Korean College of Neuropsychopharmacology* 2018;16(4):407-14. doi: 10.9758/cpn.2018.16.4.407 [published Online First: 2018/11/24]
59. Jarrett MA. Attention-deficit/hyperactivity disorder (ADHD) symptoms, anxiety symptoms, and executive functioning in emerging adults. *Psychological assessment* 2016;28(2):245-50. doi: 10.1037/pas0000190 [published Online First: 2015/06/30]
60. Howlin P, Magiati I. Autism spectrum disorder: outcomes in adulthood. *Current opinion in psychiatry* 2017;30(2):69-76. doi: 10.1097/yco.0000000000000308 [published Online First: 2017/01/10]
61. Epstein Y, Heled Y, Ketko I, et al. The effect of air permeability characteristics of protective garments on the induced physiological strain under exercise-heat stress. *The Annals of occupational hygiene* 2013;57(7):866-74. doi: 10.1093/annhyg/met003 [published Online First: 2013/02/05]
62. Davey SL, Lee BJ, Robbins T, et al. Heat stress and PPE during COVID-19: impact on healthcare workers' performance, safety and well-being in NHS settings. *The Journal of hospital infection* 2021;108:185-88. doi: 10.1016/j.jhin.2020.11.027 [published Online First: 2020/12/11]
63. Lai J, Ma S, Wang Y, et al. Factors Associated With Mental Health Outcomes Among Health Care Workers Exposed to Coronavirus Disease 2019. *JAMA network open* 2020;3(3):e203976. doi:

10.1001/jamanetworkopen.2020.3976 [published Online First: 2020/03/24]

64. Lu W, Wang H, Lin Y, et al. Psychological status of medical workforce during the COVID-19 pandemic: A cross-sectional study. *Psychiatry research* 2020;288:112936. doi: 10.1016/j.psychres.2020.112936 [published Online First: 2020/04/11]
65. Fukase Y, Ichikura K, Murase H, et al. Depression, risk factors, and coping strategies in the context of social dislocations resulting from the second wave of COVID-19 in Japan. *BMC Psychiatry* 2021;21(1):33. doi: 10.1186/s12888-021-03047-y [published Online First: 2021/01/14]
66. Kuang Y, Shen M, Wang Q, et al. Association of outdoor activity restriction and income loss with patient-reported outcomes of psoriasis during the COVID-19 pandemic: A web-based survey. *Journal of the American Academy of Dermatology* 2020;83(2):670-72. doi: 10.1016/j.jaad.2020.05.018 [published Online First: 2020/05/15]
67. Shevlin M, McBride O, Murphy J, et al. Anxiety, depression, traumatic stress and COVID-19-related anxiety in the UK general population during the COVID-19 pandemic. *BJPsych open* 2020;6(6):e125. doi: 10.1192/bjo.2020.109 [published Online First: 2020/10/20]
68. Witteveen D, Velthorst E. Economic hardship and mental health complaints during COVID-19. *Proceedings of the National Academy of Sciences of the United States of America* 2020;117(44):27277-84. doi: 10.1073/pnas.2009609117 [published Online First: 2020/10/14]
69. Tan BYQ, Chew NWS, Lee GKH, et al. Psychological Impact of the COVID-19 Pandemic on Health Care Workers in Singapore. *Annals of internal medicine* 2020;173(4):317-20. doi: 10.7326/m20-1083 [published Online First: 2020/04/07]
70. Ide K, Asami T, Suda A, et al. The psychological effects of COVID-19 on hospital workers at the beginning of the outbreak with a large disease cluster on the Diamond Princess cruise ship. *PloS one* 2021;16(1):e0245294. doi: 10.1371/journal.pone.0245294 [published Online First: 2021/01/12]
71. Cag Y, Erdem H, Gormez A, et al. Anxiety among front-line health-care workers supporting patients with COVID-19: A global survey. *General hospital psychiatry* 2021;68:90-96. doi: 10.1016/j.genhosppsych.2020.12.010 [published Online First: 2021/01/09]
72. García-Fernández L, Romero-Ferreiro V, López-Roldán PD, et al. Mental health impact of COVID-19 pandemic on Spanish healthcare workers. *Psychological medicine* 2020:1-3. doi: 10.1017/s0033291720002019 [published Online First: 2020/05/28]
73. Anda RF, Williamson DF, Escobedo LG, et al. Depression and the dynamics of smoking. A national perspective. *Jama* 1990;264(12):1541-5. [published Online First: 1990/09/26]
74. de Wit L, Luppino F, van Straten A, et al. Depression and obesity: a meta-analysis of community-based studies. *Psychiatry research* 2010;178(2):230-5. doi: 10.1016/j.psychres.2009.04.015 [published Online First: 2010/05/14]
75. Piccinelli M, Wilkinson G. Gender differences in depression. Critical review. *The British journal of psychiatry : the journal of mental science* 2000;177:486-92. doi: 10.1192/bjp.177.6.486 [published Online First: 2000/12/05]
76. McLean CP, Asnaani A, Litz BT, et al. Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness. *Journal of psychiatric research* 2011;45(8):1027-35. doi:

10.1016/j.jpsychires.2011.03.006 [published Online First: 2011/03/29]

77. Felmingham K, Williams LM, Kemp AH, et al. Neural responses to masked fear faces: sex differences and trauma exposure in posttraumatic stress disorder. *Journal of abnormal psychology* 2010;119(1):241-7. doi: 10.1037/a0017551 [published Online First: 2010/02/10]
78. McLaren HJ, Wong KR, Nguyen KN, et al. Covid-19 and women's triple burden: Vignettes from Sri Lanka, Malaysia, Vietnam and Australia. *Social Sciences* 2020;9(5):87.
79. Racine N, Hetherington E, McArthur BA, et al. Maternal depressive and anxiety symptoms before and during the COVID-19 pandemic in Canada: a longitudinal analysis. *The lancet Psychiatry* 2021 doi: 10.1016/s2215-0366(21)00074-2 [published Online First: 2021/03/28]
80. Nomura S, Kawashima T, Yoneoka D, et al. Trends in suicide in Japan by gender during the COVID-19 pandemic, up to September 2020. *Psychiatry research* 2021;295:113622. doi: 10.1016/j.psychres.2020.113622 [published Online First: 2020/12/09]
81. Hartman CA, Geurts HM, Franke B, et al. Changing ASD-ADHD symptom co-occurrence across the lifespan with adolescence as crucial time window: Illustrating the need to go beyond childhood. *Neurosci Biobehav Rev* 2016;71:529-41. doi: 10.1016/j.neubiorev.2016.09.003 [published Online First: 2016/10/30]
82. American Psychiatric Association. Diagnostic and statistical manual of mental disorders, fifth ed. Arlington, VA: American Psychiatric Pub 2013.

Figure Legends

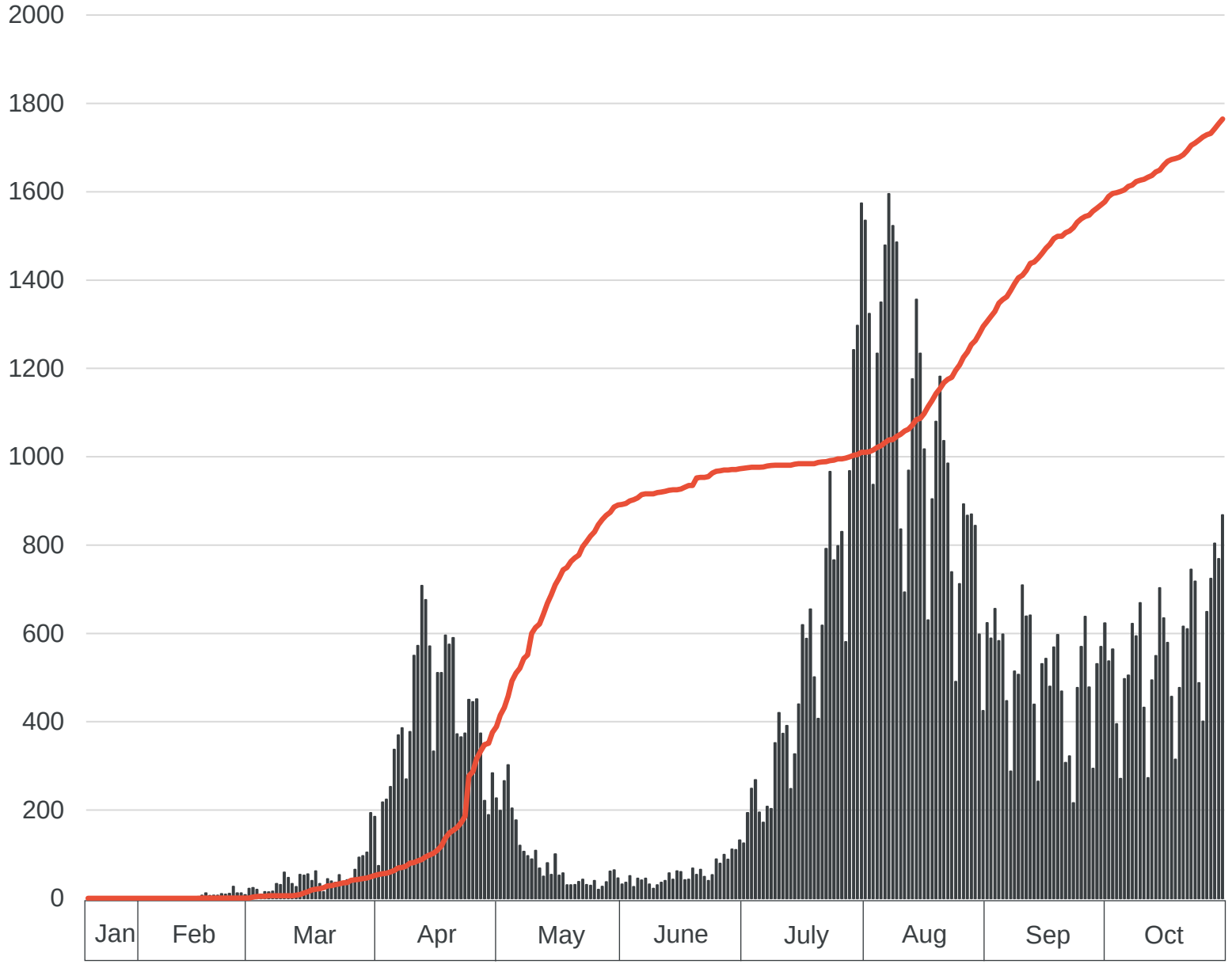
Figure 1. Epidemic curve of COVID-19 in Japan until October 2020

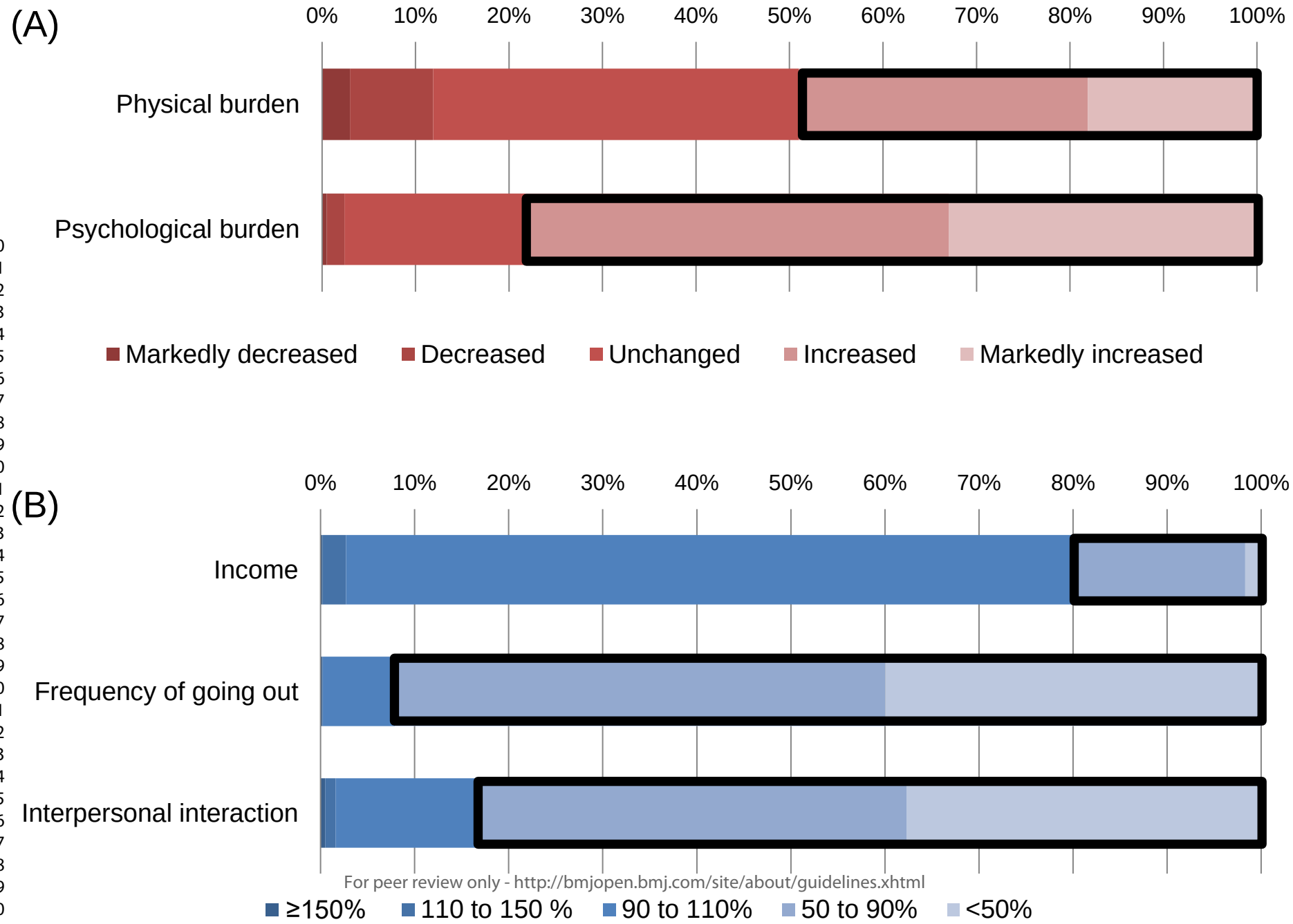
The bar graph shows the epidemic curve displaying the number of patients. The red line shows the cumulative number of deaths.

Figure 2. Changes in lifestyle among medical workers after the COVID-19 outbreak

(A) The bold square shows an increase in physical and psychological burden.

(B) The bold square shows a decrease of less than 90%.





STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	Comment	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	We have specified it in the title.	Page 1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	The abstract is structured. What was done is stated in the methods and what was found is stated in the results and conclusions.	Page 5, Line 1 to Page 6, Line 10
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	We explained the scientific background and rationale for the investigation in the introduction.	Page 5, Line 1 to Page 6, Line 10
Objectives	3	State specific objectives, including any prespecified hypotheses	We stated our hypotheses in the third paragraph of the introduction.	Page 6, Line 12–21
Methods				
Study design	4	Present key elements of study design early in the paper	We stated 'cross-sectional web-based questionnaire survey' and 'snowball sampling' in the setting and study population section of the methods.	Page 6, Line 24 to Page 7, Line 7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	We reported these data in the setting and study population section of the methods.	Page 6, Line 24 to Page 7, Line 7
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	Inclusion criteria are described in the setting and study population section of the methods.	Page 7, Line 8–13
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	All data are clearly described in the methods.	Page 7, Line 15 to Page 9, Line 21
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	Sources of data are described in the methods.	Page 7, Line 15 to Page 9, Line 21
Bias	9	Describe any efforts to address potential sources of bias	Potential sources of bias were discussed in the second to last paragraph of the discussion.	Page 18, Line 18 to Page 19, Line 9
Study size	10	Explain how the study size was arrived at	A formal sample size calculation was not performed because we had no prior information regarding the expected treatment effect.	
Quantitative	11	Explain how quantitative	Quantitative variables were	Table 1

variables		variables were handled in the analyses. If applicable, describe which groupings were chosen and why	reported using the median and interquartile range.	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Statistical methods were described in the statistical analysis section of the methods.	Page 9, Line 23 to Page 10, Line 13
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable.	
		(*c*) Explain how missing data were addressed	There was no missing data.	
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	Not applicable.	
		(*e*) Describe any sensitivity analyses	Not applicable.	
Results				
Participants	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	The numbers of individuals were reported in the last paragraph of the setting and study population.	Page 7, Line 8–13
		(b) Give reasons for non-participation at each stage	Not applicable.	
		(c) Consider use of a flow diagram	Not applicable.	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	The characteristics of study participants are shown in Table 1.	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Not applicable.	
Outcome data	15*	Report numbers of outcome events or summary measures	Outcomes are described in the results and Figure 2.	Page 11, Line 5–9, Page 12, Line 2–8, and Figure 2
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	Primary outcomes are described in the third and fourth paragraph of the results, Table 2 and Table 3.	Page 12, Line 9 to Page 14, Line 4, Table 2 and Table 3.
		(*b*) Report category boundaries when continuous variables were categorized	The category boundaries for continuous variables are shown in the methods and footnotes of Table	Page 7, Line 21 to Page 9, Line 21, Table 2, and Table 3

		2 and Table 3		
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable.	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Not applicable.	
Discussion				
Key results	18	Summarise key results with reference to study objectives	We summarized our key results in the first paragraph of the discussion.	Page 15, Line 1–6
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	We discussed limitations in the second to last paragraph of the discussion.	Page 18, Line 18 to Page 19, Line 12
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	We cautiously interpreted our results in the discussion.	Page 15, Line 7 to Page 16, Line 16
Generalisability	21	Discuss the generalisability (external validity) of the study results	The generalizability is discussed in each paragraph of the discussion.	Page 15, Line 7 to Page 18, Line 17
Other information				
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	Funding is described in the funding section	Page 20, Line 8–9

*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 www.strobe-statement.org.