Impact of the COVID-19 pandemic on patients with mental health problems and the differences among diagnostic categories

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Abstract

Background: The coronavirus disease 2019 (COVID-19) pandemic has resulted in a total upending of our daily lives. While anxiety and depression were frequently reported among the general population, the pandemic's impact on patients with mental health problems remains unknown.
Methods: A cross-sectional questionnaire survey involving 1,166 patients was conducted at one psychiatric hospital and one mental health clinic.
Results: Symptom deterioration was reported in 23% to 34% of the patients and 9% to 20% reported increase in drug dosage. No significant differences were reported in these items among diagnostic categories. Patients with *F*3 (mood disorders) reported more psychological stress during the pandemic's beginning and during the emergency. Patients with *F*2 (schizophrenia, schizotypal, and delusional disorders) did online shopping and meetings less frequently, and reported poorer adherence of 3C's, while mask management was stricter in patients with *F*4 (neurotic, stress-related, and somatoform disorders). Symptom deterioration was significantly associated with increase in drug dosage, new physical symptoms, anxiety unrelated to COVID-19, stress at the beginning of pandemic, stress during the 'state of emergency', poor adaptability to environmental change, daily life changes, decrease in sleeping time, and decrease in time spent outside.
Conclusion: One third of patients reported symptom deterioration during the pandemic, which was associated with stress and daily life changes. Patients with good adaptability to environmental changes might resilient against symptom deterioration. Providing continuous support to help patients manage their daily life in this COVID-19 era may minimize the risk of symptom deterioration.

Keywords

Anxiety, COVID-19, depression, schizophrenia, stress, risk, resilience

Introduction

The pandemic caused by the coronavirus disease 2019 (COVID-19) has had a great impact on our daily lives. The Japanese government and the World Health Organization (WHO) proposed an important notice (i.e. 'avoid the three C's': closed spaces, crowded places, and close-contact settings, and 'stay at home') to prevent the spread of COVID-19. This required a total change in our behaviors. In response to this catastrophic switch, depression and anxiety were frequently reported among the general population and one meta-analysis estimated that the pooled prevalence of depression and anxiety was 31.4% and 31.9%, respectively

(Wu et al., 2021). Some evidence showed that young people and females have a higher risk of developing a mental

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disorder caused by COVID-19 (Hammarberg et al., 2020; Varma et al., 2021), however, with respect to their vulnerability, the population with pre-existing mental health problems are of a greater concern in psychiatric clinical practices (Fiorillo & Gorwood, 2020; Kavoor, 2020; López Steinmetz et al., 2020). Indeed, an online survey revealed that people with mental health problems (mainly patients with anxiety and depression) showed more worry and fear regarding COVID-19 than their mentally healthy counterparts, and the severity of their depression deteriorated after COVID-19 (Quittkat et al., 2020). In addition, beyond psychiatric symptoms, it was reported that there was a 7-times increased risk of COVID-19 infection in patients with depression and schizophrenia, and a 1.3-times increased risk of in-hospital mortality due to COVID-19 among schizophrenic patients (Fond et al., 2021; Wang et al., 2021). Therefore, with the prolongation of the pandemic, careful management is required to prevent a relapse/recurrence in patients with mental health problems, and there is a compelling need to know how COVID-19 impacts these patients in order to identify the risk and resilience factors associated with their symptom deterioration.

In general, risk factors for relapse/recurrence in mental health problems are stress, non-adherence to treatment, residual symptoms, severity, comorbidity, family history, cognitive style, insight, and lack of support (McGrath et al., 2006; Suzuki et al., 2014). The current unpredictable state of the pandemic is causing immeasurable stress. Treatment discontinuation due to COVID-19 is another risk factor, and prevention of such discontinuation is important. Dramatic daily life changes due to COVID-19 can also increase stress, which might lead to relapse/recurrence. Indeed, our previous study revealed that 22.2% of patients who had used day care services at our psychiatric hospital, reported symptom deterioration, 16.8% reported disrupted sleeping patterns, and 42.2% felt stress during the period of the first state of emergency issued in Japan due to COVID-19 (April 7–May 25, 2020) when day care services were stopped and they needed to stay at home (Koreki et al., 2020). It also revealed that deterioration of their psychiatric symptoms was significantly associated with whether they could maintain their regular routine in their daily life (Koreki et al., 2020).

Resilience is another key issue during the COVID-19 pandemic and can be broadly defined as the capacity of a dynamic system to adapt successfully to disturbances that threaten the system function, viability, or development (Masten, 2015; Ungar & Theron, 2020). In response to the COVID-19 pandemic, we need to adapt to our new lifestyles. Resilience can minimize the impact of COVID-19 (Blanc et al., 2021; Lenzo et al., 2020). There are some studies regarding resilience against the COVID-19 pandemic among the general population (Kimhi et al., 2020; Lenzo et al., 2020), general workers (Coulombe et al., 2020), and healthcare workers (Awano et al., 2020; Pietrzak et al., 2020), which reveal enough support, coping styles, personal interests, general enthusiasm, family functioning, trait resilience, social participation, economic stability, high income, and trust in healthcare institutions as factors that influence development of resilience.

However, it is still unknown how patients with mental health problems deal with COVID-19, how their mental states change, and which factors are associated with their relapse/recurrence. In the present study, a cross-sectional questionnaire was conducted to address this question.

Methods

A self-reported questionnaire was distributed in the authors' consultation room for outpatients at one psychiatric hospital and one mental health clinic between October 8 and November 4, 2020. In regard to the nature of our hospital, the majority of outpatients were patients with more severe mental conditions, such as schizophrenia, bipolar disorder, and psychotic depression, with a history of hospitalization. In contrast, our clinic focuses on outpatient therapies for patients with milder mental conditions, such as mood disorders and neuroses, as a primary care setting. Most patients, including those who achieved remission and maintenance therapy for relapse prevention, had frequented our hospital or clinic before the COVID-19 pandemic. During the pandemic, neither facility offered virtual appointments. We distributed questionnaires to the outpatients who visited regularly and excluded patients deemed unfit to fill them out by the respective attending psychiatrists. Each patient filled in this questionnaire only once. The questionnaire was originally developed to describe their current clinical and daily life situations associated with COVID-19. It consisted of six parts (general information, mental condition, stress and resilience, daily life change, hygiene and money, and hospital visit) and a total of 48 items. Each item has been described in Table 1. In order to clarify their diagnosis, the questionnaires were anonymized but consolidated with their medical records, and their diagnoses were confirmed by psychiatrists (YM and AK). Some data were converted to numbers for our analysis. For example, the choices ('Very Much/Much/Not so much/Not at all') were converted to ordinary data [1, 2, 3, 4], respectively. Subsequently, the questionnaire responses were analyzed as follows.

One of our study interests was the differences among patients with mental health problems. Here, patients were recategorized into four groups ($F2$: schizophrenia, schizotypal, and delusional disorders, $F3$: mood disorders, $F4$: neurotic, stress-related and somatoform disorders, and Others) based on the International Statistical Classification of Diseases and Related Health Problems (ICD)-10 (World Health Organization, 2004). The Kruskal-Wallis test was performed for cases where the data were ordinal variables, the χ^2 test was performed for cases where the data were

categorical variables, and analysis of variance (ANOVA) was performed for cases where the data were continuous variables. Bonferroni correction was used for post-hoc analyses. As there were a large number of items (48 items) in the questionnaires and each item was analyzed, $p < .001$ was considered significant.

Another point of interest was the factors that were significantly associated with the relapse/recurrence of the patients' symptoms. A key item of the questionnaire was the item regarding their relapse/recurrence ('Did your mental condition get worse due to COVID-19?'). First, univariate analyses were conducted for each item, and subsequently a logistic regression analysis as a multivariate analysis was conducted with age, sex, diagnostic category, hospital/clinic, and significant items in univariate analyses as dependent variables. As most of the items were ordinary variables with four scale points or less (Carifio & Perla, 2007), we entered most of the data into a logistic regression analysis as binary data in the following way. If items had four choices (for e.g. 'Very Much/Much/Not so much/Not at all'), the data was split at the point between the second and third from the left. For items regarding sleeping time and time spent outside, the data was split by decreased or not decreased sleeping time and time spent outside. These splitting points were determined using clinical implications. As for the item regarding new physical symptoms, some patients wrote down physical problems such as sleeplessness. In that case, their answers were relabeled. In the multivariate analysis, we analyzed the data of all diagnostic groups and $p < .05$ was considered significant. In addition, to discuss more diagnostically specific factors, a diagnostic stratified analysis was conducted. Statistical analyses were conducted using R (4.0.2). Ethical approval was obtained from the Institutional Ethical Review Board of the Shimofusa Psychiatric Medical Center (020917003). Informed consent was obtained in the way that the submission of questionnaires signaled their agreement.

Results

Questionnaires were collected from 1,166 patients (response rate: 91.2% (1,166/1,278)). It included patients with $F2$ ($n = 292$), $F3$ ($n = 562$), $F4$ ($n = 161$), and others ($n = 151$). Most patients lived in Chiba prefecture, which is near Tokyo.

Distribution of answers and differences among diagnostic categories

The distribution of the patients' answers and the differences among diagnostic categories are shown in Table 1. The patients' general background showed a significant difference in hospital/clinic visits ($p < .001$) and employment ($p < .001$) among diagnoses, which was simply due to the

fact that $F2$ is generally more severe than other diagnostic categories. Living with elderly people was also different ($p < .001$), which might be due to the type of their caregivers.

In the section regarding their mental health condition, patients with $F2$ stated that they started to go to the hospital earlier than those in other diagnostic categories ($p < .001$) and had frequent admission history ($p < .001$). The mental condition before COVID-19 pandemic was significantly unstable in patients with $F2$ than in those from other diagnostic categories. These findings were simply reflected in the fact that patients with $F2$ had more severe symptoms and the onset was earlier than that in other diagnostic categories. Interestingly, the difference in their symptom deterioration or increase in drug dosage was not significant in the present study. Here, 23% to 34% of patients reported symptom deterioration and 9% to 20% reported increase in their drug dosage. Surprisingly, some patients reported symptom improvement (4%–6%) and decrease in their drug dosage (3%–5%). With regard to anxiety, there was a significant difference unrelated to COVID-19 ($p < .001$), and more anxiety was seen in patients with $F3$. In contrast, anxiety related to COVID-19 was not significant. No significant difference in hallucinations or new physical symptoms was found, although 1% to 7% reported COVID-19 related hallucinations and 6% to 13% reported new physical symptoms.

In the section regarding stress and resilience, there were significant differences in stress at the beginning of the COVID-19 pandemic and during the first state of emergency (both $p < .001$), where patients with $F3$ felt more stress than those in other diagnostic categories. In contrast, no significant difference was found in the items regarding adaptation of daily life during the pandemic, and interestingly, the majority of patients (79%–91%) reported that they are already used to their daily life during the pandemic.

In the section regarding impact on their daily life, more than half of the patients reported a change in their daily life but that they could maintain their regular routine even during the pandemic. No group differences were found in these items. Some patients reported decrease in sleeping time (8%–16%) and unhealthy eating habits (21%–28%), weight gain (25%–30%), and increased frequency of using a delivery food service (7%–13%), but no group difference was found. Patients with $F3$ reported a significant decrease in time spent outside compared to patients in other diagnostic categories ($p < .001$). Patients with $F2$ engaged in online shopping and attended online meetings less frequently than patients in other diagnostic categories (both $p < .001$).

In the section regarding hygiene and money, a small number of patients (1%–6%) reported the presence of patients with COVID-19 around them. A majority of patients (69%–81%) checked information regarding COVID-19 more than once a day, but no group difference

Table 1. The questionnaire and the differences of answers among diagnoses.

Item	Responses		F2 (n = 292)	F3 (n = 562)	F4 (n = 161)	Others (n = 151)	p-Value	Post hoc
General information								
Hospital/clinic	Hospital/clinic	%	68/32	16/84	12/88	52/48	<.001 (‡)	F2–F3, F2–F4, F3-Others, F4-Others
Age	( )	Mean (SD)	48 (±13)	51 (±14)	49 (±15)	50 (±19)	.026a	—
Sex	Male/female	%	49/51	48/52	39/61	60/40	.004b	—
Prefecture	Chiba/Tokyo/others	%	99/0/1	97/2/1	96/1/3	94/3/3	.040b	—
Living status	Living alone/together	%	21/79	19/81	11/89	30/70	.008b	—
With elderly people	Yes/no	%	45/55	29/71	30/70	37/63	<.001b	F2–F3
With kids	Yes/no	%	18/82	36/64	49/51	18/82	<.001b	F2–F3, F2–F4, F3-Others, F4-Others
Another hospital visit	Yes/no	%	39/61	48/52	47/53	45/55	.130b	—
Employment	Yes/no	%	32/68	57/43	64/36	40/60	<.001b	F2–F3, F2–F4, F4-Others
Mental health								
How old were you when you started going to the hospital?	( )	Mean (SD)	32 (±13)	43 (±15)	42 (±16)	39 (±21)	<.001a	F2–F3, F2–F4, F2-Others, F3-Others, F4-Others
Have you ever been hospitalized at psychiatric hospitals?	Yes/no	%	67/33	23/77	12/88	41/59	<.001b	F2–F3, F3-Others
How was your mental health before COVID-19?	Quite stable/stable/unstable/quite unstable	%	39/34/23/4	27/30/32/10	33/33/30/31	42/27/27/5	<.001	F2–F3, F3-Others
Did your mental condition get worse due to COVID-19?	Much worse/worse/no change/rather better	%	4/19/72/6	6/28/63/4	5/27/63/6	7/21/69/4	.014	—
Did you increase your drug dosage (including drug use as needed) due to COVID-19?	Dramatically increased/increased/no change/rather decreased	%	1/8/88/3	2/11/84/3	2/14/79/5	4/16/77/4	.136	—
Did you have difficulty in continuing your medication due to COVID-19?	Always/often/rarely/never	%	1/4/27/69	1/3/22/75	1/8/21/70	1/5/20/73	.258	—
Do you experience hallucinations about COVID-19 (if you do have hallucinations)?	Yes/no	%	4/96	1/99	5/95	7/93	.040b	—
Do you have any new physical symptoms after beginning of the COVID-19 pandemic?	Yes/no	%	6/94	9/91	13/87	6/94	.089b	—
How anxious are you about COVID-19?	Very much/much/not so much/not at all	%	9/43/26/23	10/52/24/14	10/48/26/16	13/34/29/25	.006	—
How anxious are you in general, even without COVID-19?	Very much/much/not so much/not at all	%	9/43/26/22	16/46/25/13	12/46/28/13	19/30/26/25	<.001	F2–F3
Stress and resilience								
How stressed were you at the beginning of the COVID-19 pandemic?	Very much/much/not so much/not at all	%	14/43/25/18	24/48/20/9	18/53/16/13	15/45/23/17	<.001	F2–F3, F3-Others
How stressed were you during the 'state of emergency'? Due to COVID-19 (April–May)?	Very much/much/not so much/not at all	%	18/43/24/15	30/43/21/7	22/52/14/12	24/42/18/16	<.001	F2–F3
How stressed are you at present due to COVID-19?	Very much/much/not so much/not at all	%	11/41/28/20	9/52/29/10	7/53/29/11	10/38/29/23	.007	—
How used to are you to your daily life under the COVID-19 pandemic?	Very much/much/not so much/not at all	%	16/65/12/7	15/71/11/4	19/72/8/2	18/61/16/5	.156	—
How well do you manage your daily life to avoid stress due to COVID-19?	Very much/much/not so much/not at all	%	9/37/35/18	7/46/35/12	10/40/38/12	8/29/43/20	.010	—
How good are you at adapting to environmental change?	Very much/much/not so much/not at all	%	4/32/51/13	4/31/50/15	6/29/52/13	6/30/49/15	.949	—

(Continued)

Table I. (Continued)

Item	Responses	%	F2 (n=292)	F3 (n=562)	F4 (n=161)	Others (n=151)	p-Value	Post hoc
Daily life changes								
How much did your daily life change due to COVID-19?	Very much/much/not so much/not at all	%	10/44/30/16	20/46/24/10	18/51/21/11	13/47/23/17	.156	—
How well did you maintain your regular routines even with the pandemic?	Very much/much/not so much/not at all	%	28/47/18/8	27/48/19/6	32/45/18/5	29/46/19/7	.661	—
How did your sleep time change after the pandemic?	Increased/no change/decreased	%	12/80/8	11/75/13	8/80/13	6/78/16	.039	—
Did your eating habits get worse due to COVID-19?	Very much/much/not so much/not at all	%	3/18/47/32	6/20/43/31	2/26/42/29	5/16/41/37	.313	—
Did you use food delivery services more than you did before due to COVID-19?	Yes/no	%	7/93	13/87	8/92	9/91	.044[b]	—
How did your body weight change after the pandemic?	Increased/no change/decreased	%	26/65/10	30/57/13	25/62/13	26/61/13	.719	—
How did your time out of the house change after the pandemic?	Increased/no change/decreased	%	3/52/46	2/31/68	1/37/63	2/43/55	**<.001**	F2–F3
Did you do online shopping more than before due to COVID-19?	Yes/no	%	17/83	40/60	36/64	24/76	**<.001**[b]	F2–F3, F2–F4
Did you start meeting anyone online (using Zoom, Skype, etc.)? Due to COVID-19?	Yes/no	%	6/94	22/78	16/84	9/91	**<.001**[b]	F2–F3
Hygiene and support money								
Are you around any patient/s with COVID-19?	Yes/no	%	1/99	2/98	6/94	2/98	.007[b]	—
How often do you check information regarding COVID-19?	Several times per day/once per day/2 to 3 times per week/once per week or less	%	27/45/13/15	24/57/12/7	22/50/18/9	24/45/17/14	.148	—
How much do you keep the '3C's' in mind?	Very much/much/not so much/not at all	%	28/54/13/5	41/50/8/2	48/45/5/3	38/44/10/8	**<.001**	F2–F3, F2–F4,
How often do you wear a mask when you go out?	Always/often/rarely/never	%	75/18/6/1	84/13/2/1	90/8/1/1	80/16/1/3	**<.001**	F2–F4
How often do you change your mask?	Everyday/several times/1 to 2 times per week/once per week or less	%	50/26/11/13	66/23/6/5	73/22/4/1	60/24/10/7	**<.001**	F2–F3, F2–F4
How often do you wash your mask (if you continue to use the same mask)?	Always/often/rarely/never	%	43/20/11/26	60/19/7/14	64/19/6/12	54/21/8/18	**<.001**	F2–F3, F2–F4
How uncomfortable do you feel when you wear a mask?	Very much/much/not so much/not at all	%	20/46/21/13	25/46/20/9	21/41/19/19	22/39/17/21	.007	—
How often do you wash your hands and gargle your throat?	Always/often/rarely/never	%	61/30/8/2	73/25/2/1	79/21/1/0	65/24/9/2	**<.001**	F2–F3, F2–F4
Have you received support money associated with COVID-19 from the government yet?	Yes/no	%	92/8	96/4	96/4	90/10	.052[b]	—
How did/will you use the support money (if you do not mind answering)?	Saving/living expenses/hobby/others	%	29/56/13/9	23/61/14/6	21/63/12/10	30/50/12/12	.768[b]	—
Hospital visit								
How stressed are you when you visit the hospital during COVID-19?	Very much/much/not so much/not at all	%	10/27/37/26	5/34/39/22	10/35/32/23	7/27/32/34	.093	—
How used to are you to visiting the hospital under COVID-19?	Very much/much/not so much/not at all	%	20/61/11/8	24/66/8/2	25/63/8/4	26/48/16/10	.008	—
How did you reconsider your method to visit the hospital?	Very much/much/not so much/not at all	%	6/29/40/24	5/34/39/22	6/37/33/24	6/37/32/25	.788	—
What part of the visit did you reconsider?	Way of visit/visit interval/wait time or method/others	%	22/19/52/13	21/19/66/7	17/23/63/10	16/17/66/12	.654[b]	—
Did you refrain from visiting a new hospital due to COVID-19?	Always/often/rarely/never	%	6/15/27/52	7/22/25/46	10/25/24/41	6/20/21/53	.014	—

[a]Items were analyzed using ANOVA.
[b]Items using χ^2 test. Other items were analyzed using Kruskal-Wallis test. Post-hoc analysis was the Bonferroni correction.
Bold values indicate statistical significance.

was found. Patients with *F*2 kept the '3C's' in mind, wore a mask, changed their mask, or washed their mask less frequently than patients with *F*3 and *F*4 (*p* < .001 for all these items). Most patients (89%–99%) always washed their hands and gargled, but it was less frequent in patients with *F*2. Most patients received the Japanese government benefits, and their dominant personal use was for living expenses.

In the section regarding hospital visits, some patients (34%–45%) felt stress during hospital visits and 21% to 35% refrained from new visits, but 74% to 90% were already used to hospital visits during the pandemic. No group differences were found in these items. Majority of the patients (52%–66%) reported that they reconsidered their hospital visit.

Significant factors associated with symptom deterioration in the diagnostic stratified analysis

Univariate analysis revealed that symptom deterioration was associated with various factors (Tables 2 and 3). In all samples, the logistic analysis revealed that symptom deterioration was significantly associated with increase of drug dosage (*p* < .001, Odds ratio (OR): 9.2 [95% Confidence interval (CI): 5.4–16.0]), new physical symptoms (*p* = .003, OR: 3.0 [1.5–6.1]), anxiety unrelated to COVID-19 (*p* = .010, OR: 1.8, [1.2–2.7]), stress at the beginning of the pandemic (*p* = .042, OR: 1.9 [1.03–3.5]), stress during the first state of emergency (*p* = .002, OR: 3.1 [1.5–6.5]), adaptability to environmental change (*p* = .015, OR: 0.6 [0.4–0.9]), daily life change (*p* < .001, OR: 2.6 [1.7–4.1]), decrease in sleeping time (*p* < .001, OR: 3.1 [1.8–5.2]), and decrease in time spent outside (*p* = .012, OR: 1.7 [1.1–2.5]).

In patients with *F*2, symptom deterioration was significantly associated with new physical symptoms (*p* < .005, OR: 16.0 [2.8–135.8]), stress at the beginning of the pandemic (*p* = .045, OR: 4.8 [1.1–2.5]), unhealthy eating habits (*p* = .008, OR: 3.2 [1.4–7.8]), and decrease in time spent outside (*p* = .004, OR: 3.5 [1.5–8.4]).

In patients with *F*3, their symptom deterioration was significantly associated with increase in drug dosage (*p* < .001, OR: 14.6 [6.2–38.4]), anxiety unrelated to COVID-19 (*p* = .004, OR: 2.6, [1.4–4.9]), stress during the first state of emergency (*p* = .015, OR: 3.6 [1.3–10.4]), daily life management (*p* = .046, OR: 1.8 [1.01–3.2]), adaptability to environmental change (*p* = .008, OR: 0.5 [0.3–0.8]), daily life change (*p* < .001, OR: 3.6 [1.9–7.1]), maintaining regular routines (*p* < .001, OR: 0.3 [0.2–0.6]), and decrease in sleeping time (*p* = .014, OR: 2.7 [1.2–6.2]).

In patients with *F*4, symptom deterioration was significantly associated only with increase in drug dosage (*p* < .001, OR: 70.9 [11.3–1590.0]).

Discussion

To our knowledge, this is the first big survey aimed at unveiling the impact of COVID-19 on clinical conditions and daily life on patients with mental health problems. After more than half a year since the onset of the COVID-19 pandemic, we faced miserable social situations involving lack of materials (such as masks and alcohol for disinfection), spread of misinformation, absence of vaccines, and a dramatic change in daily life. During this time, 23% to 34% of patients with pre-existing mental problems reported symptom deterioration and 9% to 20% reported an increase in their drug dosage. One study conducted during the early stage of COVID-19 revealed that patients with schizophrenia and mood disorders were not reporting symptom deterioration yet (Pinkham et al., 2020). This may indicate that long-term stress of COVID-19 affected their symptoms. Indeed, approximately half of the patients still did not feel stress related to COVID-19 at the time of the survey. In contrast, our survey was conducted approximately 8 months after the beginning of the pandemic. During this period, there were dramatic changes in our life style, including adjustment to the first state of emergency declared by the Japanese government. Of course, regardless of the pandemic, relapse and recurrence occur; even without disruptions in medication adherence, and the rates are estimated to be 27%/year for schizophrenia, 20.9%/40 weeks for depression, 21.9%/year for bipolar disorder, and 23.5%/2 years for anxiety disorders in meta-analyses (Kato et al., 2021; Leucht et al., 2012; Scholten et al., 2013; Vázquez et al., 2015). However, although our study had subjective evaluations, we believe the pandemic affected the patients' deterioration because deterioration was significantly associated with stress relating to COVID-19. Furthermore, our analyses demonstrated the differences in the impact of COVID-19 on their clinical conditions and daily lives.

Several differences among diagnoses were found in the present study. First, stress at the beginning of the pandemic and during the first state of emergency was more severe in patients with *F*3 than in other patients. This might be due to depression-specific pessimistic thoughts regarding the past as a recall bias. A smaller change in the time spent outside for patients with *F*2 might be reflected in their lower frequency of time spent outside even before the COVID-19 pandemic and more difficulty with behavioral changes depending on the social situation caused due to their negative symptoms and cognitive impairment. Patients with *F*2 engaged in online shopping and attended online meetings less frequently, and this may be due to their cognitive dysfunction as well as their negative symptoms. We should encourage and support their use of online services because it is key to survival during the pandemic. There were significant differences in items regarding hygiene (3C's, mask, wash, and gargle). Poorer hygiene was seen in patients with *F*2, while better hygiene was

Table 2. Symptom deterioration in the multivariate analysis.

Item	Univariate	Multivariate	
	All	All (n = 1,166)	
	p Value	p Value	OR [95% CI]
General information			
Diagnosis	.014		
Hospital/clinic	.001	.534	1.2 [0.7–2.1]
Age	.178	.345	1.0 [1.0–1.0]
Sex	.038	.542	0.9 [0.6–1.3]
Prefecture	.147		
Living status	.031		
Living with elderly people	.071		
Living with kids	.823		
Another hospital visit	.084		
Employment	.177		
Mental Health			
First visit to hospital	.836		
Admission history	.027		
Pre-mental condition	<.001	.364	1.2 [0.8–1.7]
Increases of drug dosage	<.001	**<.001**	**9.2 [5.4–16.0]**
Difficulty continuing medications	<.001	.365	1.2 [0.8–1.7]
Hallucinations	.400		
New physical symptoms	<.001	**.003**	**3.0 [1.5–6.1]**
Anxiety related to COVID-19	<.001	.262	1.3 [0.8–2.0]
Anxiety unrelated to COVID-19	<.001	**.010**	**1.8 [1.2–2.7]**
Stress and resilience			
Stress at the beginning of the pandemic	<.001	**.042**	**1.9 [1.03–3.5]**
Stress during the 'state of emergency'	<.001	**.002**	**3.1 [1.5–6.5]**
Stress at present	<.001	.108	1.5 [0.9–2.4]
Adaptation to daily life during the pandemic	<.001	.601	0.9 [0.5–1.5]
Daily life management	<.001	.134	1.4 [0.9–2.0]
Adaptability to environmental change/s	<.001	**.015**	**0.6 [0.4–0.9]**
Daily life changes			
Daily life changes	<.001	**<.001**	**2.6 [1.7–4.1]**
Maintaining regular routines	<.001	.073	0.7 [0.4–1.04]
Decreases in sleep duration	<.001	**<.001**	**3.1 [1.8–5.2]**
Unhealthy eating habits	<.001	.263	1.3 [0.8–1.9]
Use of Food delivery service	.007		
Weight gain	.798		
Decrease in time spent outside	<.001	**.012**	**1.7 [1.1–2.5]**
Online shopping	.003		
Online meetings	.439		
Hygiene and support money			
Being around COVID-19 patients	.865		
Information check	<.001	.462	1.2 [0.8–1.9]
Three C's	<.001	.911	0.96 [0.5–2.0]
Wearing a mask	.074		
Changing a mask	.046		
Washing a mask	.268		
Discomfort wearing a mask	<.001	.221	1.3 [0.9–1.9]
Gargling and hand washing	.036		
Government benefits	.270		
Personal use of the benefits	.037		
Hospital visit			
Stress during hospital visits	<.001	.550	1.1 [0.8–1.6]
Adaptation of hospital visit under the pandemic	.006		
Reconsideration of hospital visits	<.001	.955	0.99 [0.7–1.5]
Details of reconsideration	.002		
Refrainment from visiting a new hospital	<.001	.716	1.0 [1.0–1.0]

Note. Logistic regression analyses in each diagnostic category were conducted with symptom deterioration as an independent variable, and age, sex, diagnostic category, hospital/clinic, and significant items in univariate analyses as dependent variables. Bold values in the multivariate analyses indicate statistical significance.

Table 3. Symptom deterioration in the diagnostic stratified multivariate analysis.

Item	Univariate			Multivariate					
	F2	F3	F4	F2 (n = 292)		F3 (n = 562)		F4 (n = 161)	
	p Value	p Value	p Value	p Value	OR [95% CI]	p Value	OR [95% CI]	p Value	OR [95% CI]
General information									
Diagnosis									
Hospital/clinic	.109	.379	.396	.500	1.3 [0.6–3.1]	.788	1.1 [0.6–2.3]	.468	1.9 [0.4–16.0]
Age	.507	.059	.648	.102	1.0 [0.9–1.01]	.483	1.0 [1.0–1.0]	.337	1.0 [0.9–1.02]
Sex	.587	.251	.663	.748	1.1 [0.5–2.5]	.610	0.9 [0.5–1.5]	.738	0.8 [0.3–2.3]
Prefecture	.737	.802	.433						
Living status	.744	.004	.254						
Living with elderly people	.639	.064	.472						
Living with kids	.438	.995	.762						
Another hospital visit	.127	.029	.468						
Employment	.152	.166	.156						
Mental health									
First visit to hospital	.872	.025	.445						
Admission history	.231	.431	.076						
Pre-mental condition	.029	.085	.024						
Increases of drug dosage	.027	<.001	<.001	**.005**	**16.0 [2.8–135.8]**	**<.001**	**14.6 [6.2–38.4]**	**<.001**	**70.9 [11.3–1,590.0]**
Difficulty continuing medications	.014	<.001	.009			.496	1.7 [0.4–7.8]		
Hallucinations	.384	.212	.385						
Stress and resilience									
New physical symptoms	<.001	<.001	<.001	.919	1.1 [0.4–3.2]	.217	2.0 [0.7–5.9]	.077	4.3 [0.9–23.4]
Anxiety related to COVID-19	<.001	<.001	<.001			.298	1.4 [0.7–2.9]		
Anxiety unrelated to COVID-19	<.001	<.001	.011	.408	1.6 [0.5–4.9]	**.004**	**2.6 [1.4–4.9]**	.089	2.9 [0.9–11.0]
Stress at the beginning of the pandemic	<.001	<.001	<.001	**.045**	**4.8 [1.1–2.5]**	.216	1.8 [0.7–4.7]	.973	1.0 [0.2–6.0]
Stress during the 'state of emergency'	<.001	<.001	<.001	.268	3.1 [0.5–2.8]	**.015**	**3.6 [1.3–10.4]**	.345	2.5 [0.4–18.1]
Stress at present	<.001	<.001	<.001	.252	2.2 [0.6–8.7]	.215	1.5 [0.8–3.1]	.871	0.9 [0.3–3.3]
Adaptation to daily life during the pandemic	.034	<.001	.031			.429	1.4 [0.6–3.2]		
Daily life management	.126	<.001	.005			**.046**	**1.8 [1.01–3.2]**		
Adaptability to environmental change/s	.667	<.001	.080			**.008**	**0.5 [0.3–0.8]**		

Table 3. (Continued)

Item	Univariate			Multivariate					
	F2	F3	F4	F2 (n = 292)		F3 (n = 562)		F4 (n = 161)	
	p Value	p Value	p Value	p Value	OR [95% CI]	p Value	OR [95% CI]	p Value	OR [95% CI]
Daily life changes									
Dailey life changes	<.001	<.001	.002	.089	2.2 [0.9–5.9]	**<.001**	**3.6 [1.9–7.1]**		
Maintaining regular routines	.424	<.001	.080			**<.001**	**0.3 [0.2–0.6]**		
Decreases in sleep duration	.228	<.001	.004			**.014**	**2.7 [1.2–6.2]**		
Unhealthy eating habits	<.001	<.001	.070	**.008**	**3.2 [1.4–7.8]**	.690	0.9 [0.5–1.6]		
Use of Food delivery service	.733	.003	.770						
Weight gain	.073	.945	.051						
Decreases in time spent outside	<.001	<.001	.013	**.004**	**3.5 [1.5–8.4]**	.603	1.2 [0.7–2.2]		
Online shopping	.643	.147	.110						
Online meetings	.383	.883	.708						
Hygiene and support money									
Being around COVID-19 patients	.383	.773	.396						
Information check	.045	.002	.757						
Three C's	.008	.014	.329						
Wearing a mask	.398	.548	.226						
Changing a mask	.098	.540	.682						
Washing a mask	.702	.772	.782						
Discomfort wearing a mask	.006	.002	.247						
Gargling and hand washing	.112	.683	.501						
Government benefits	.151	.252	.396						
Personal use of the benefits	.433	.660	.072						
Hospital visit									
Stress during hospital visits	<.001	<.001	.102	.100	2.0 [0.9–4.4]	.967	1.0 [0.6–1.7]		
Adaptation of hospital visit under the pandemic	.853	.002	.129						
Reconsideration of hospital visits	.139	.086	<.001					.373	1.6 [0.6–4.3]
Details of reconsideration	.020	.202	.175						
Refrainment from visiting a new hospital	.004	<.001	.002			.533	1.2 [0.7–2.0]		

Logistic regression analyses in each diagnostic category were conducted with symptom deterioration as an independent variable, and age, sex, diagnostic category, hospital/clinic, and significant items in univariate analyses as dependent variables. Bold values in the multivariate analysis indicate statistical significance.

seen in patients with *F*4. Poor hygiene in *F*2 is well-known and we revealed that this clinical issue remained even during the pandemic when individual hygiene management was strongly promoted (Brewer et al., 1996). It may contribute to an increased risk of COVID-19 in patients with schizophrenia (Wang et al., 2021). Good hygiene in *F*4 could be obsessive but paradoxically adaptive to the COVID-19 pandemic.

Some significant factors associated with symptom deterioration were found along with different factors among the diagnostic categories. It is not surprising that symptom deterioration was associated with increased drug dosage. The association between symptom deterioration and increase in drug dosage was higher in *F*4 than in other diagnostic categories. It might be partially reflected in the high risk of benzodiazepine dependence in the pharmacological treatment of anxiety (O'Brien, 2005), and in the limitation of cognitive behavioral therapy in Japan, which may be a challenge for the future (Nakajima et al., 2020). New physical symptoms were seen in *F*2. This item was intended to assess somatization, although the question was indirect and inaccurate. Somatization is thought to be seen when adaptive coping, such as verbalization and exercise is not carried out (García-Sierra et al., 2020). Poorer ability to develop an alternative coping strategy during the pandemic, such as online meetings and alternative exercise among *F*2 patients may have resulted in their somatic symptoms. Anxiety unrelated to COVID-19 was significantly associated with symptom deterioration in *F*3. Compared to anxiety related to COVID-19-which is anxiety regarding the future, and is neurotic rather than depressive, the association with unrelated anxiety might be reflected in one feature of mood disorders, which is usually regarding the past (Ito et al., 2019). In contrast, the association with related anxiety was not found in *F*4, probably due to the timing when the study was conducted, which is when people were slightly optimistic regarding COVID-19 due to a decline in the number of patients with COVID-19 in Japan.

With regard to other factors associated with symptom deterioration, stress at the beginning of the pandemic was significant in *F*2, while stress during the first state of emergency was significant in *F*3. We speculate that patients with *F*2 could be sensitive to initial slight changes in society, possibly due to their aberrant salience and delusion of self-reference. Adaptability to environmental change reduced the risk of symptom deterioration in *F*3. It is in line with the concept of resilience as a personal trait in which individuals are able to adapt to adversity as a resilience factor (Coulombe et al., 2020; Lee et al., 2013). In contrast, daily life management showed a rather positive association with symptom deterioration in *F*3, although this item was initially considered a potential resilience factor. The order in which we thought this happened was that their daily life management worked as a protective shield against symptom deterioration. However, our findings implied the reverse; their symptom deterioration made them manage their daily life to avoid stress. This suggests that patients might have ended up running behind on tasks and chores while being in an unpredictable situation. Daily life changes and decrease in sleeping time were significantly associated with symptom deterioration in *F*3, while maintaining the regular routine was a strong resilience factor. Advice regarding these points would be helpful for prevention of symptom deterioration during this seemingly endless situation of COVID-19. In *F*2, unhealthy eating habits and decrease in time spent outside were significantly associated with symptom deterioration. In general, patients with schizophrenia follow unhealthy diets due to various reasons (such as poor self-care capability and the adverse effects of antipsychotics (Dipasquale et al., 2013), but the association seen in the present survey might be due to a dysfunction of self-care capability under the condition where much stricter self-control is required. The decrease in time spent outside may lead to prolonged social withdrawal, which can lead to a risk of relapse in schizophrenia (Robinson et al., 1999; Suzuki et al., 2014). Our previous survey after the discontinuance of day care services due to COVID-19 showed that 22.2% of patients reported symptom deterioration (Koreki et al., 2020).

Surprisingly, some patients reported symptom improvement and decreased drug dosage. As the ratio of this kind of improvement was low in our sample, it was not specifically analyzed in the present study. However, we heard some interesting claims from the patients in our clinic. Some patients claimed that work from home reduced their work stress dramatically. Working at the office forced them to do hard commuting and they had limited work self-control. Other patients claimed that wearing a mask mitigated their social anxiety. We also speculated that 'staying at home' excused patients' social withdrawal from criticism.

Our strengths were the use of a substantial sample size and psychiatrists-confirmed diagnostic categories based on each medical record. In contrast, there are several limitations to this study. First, causality cannot be inferred from the statistical associations, given the study's cross-sectional design; thus, further longitudinal study is required. Second, we did not distribute questionnaires to patients deemed unfit to fill them out by their respective attending psychiatrists. Therefore, patients with quite severe conditions were excluded, possibly resulting in underestimation of our findings. Third, our questionnaire was self-reported and had a limitation on accuracy, especially for the items regarding symptom deterioration in schizophrenic patients with a lack of insight. In addition, our questionnaire was originally developed to describe the patients' current clinical and daily life situations associated with COVID-19. Although each item itself was important, validation was limited. Fourth, recall bias may

have affected the responses to items regarding the past, such as stress at the beginning of the pandemic and during the first state of emergency. Fifth, our analysis in the present study was conducted based on large diagnostic categories (i.e. *F*2, *F*3, and *F*4), and each group was slightly heterogeneous. Further studies to investigate the subcategories are necessary. Sixth, the present study did not include data from healthy people and did not examine the difference between healthy people and patients with mental health problems. Seventh, there could be various confounding factors which were not assessed in the present study. Further study is required to investigate these factors. Eighth, since only one hospital and one clinic were surveyed in this study, the findings may not be generalizable. Ninth, although the COVID-19 pandemic still remains a problem and its severity status keeps fluctuating, our present survey was conducted at one time-point. Therefore, this is also a limitation regarding the generalizability of our findings.

In conclusion, according to our findings, one third of the patients reported symptom deterioration due to the COVID-19 pandemic and their deterioration was significantly associated with stress due to the pandemic and daily life changes. Patients with good adaptability to environmental changes were resilient against symptom deterioration. These findings may help mental health workers to support patients with mental health problems. The COVID-19 pandemic is ongoing, and additional peaks are anticipated. Furthermore, novel infectious diseases and changes in social conditions (e.g. wars) may bring about additional major life changes. We should provide patients with continuous support to help them manage their daily life to minimize the risk of symptom deterioration. We should also support their hygiene management, especially the patients with *F*2.

Author contributions

YM, MO, JN, and AK designed this study. SK, MO, TO, and AK managed the research environment of this study. All authors contributed to data collection. YM and AK conducted the analyses. YM and AK wrote the first draft, and all authors read and approved the final manuscript.

Data availability

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

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References

Awano, N., Oyama, N., Akiyama, K., Inomata, M., Kuse, N., Tone, M., Takada, K., Muto, Y., Fujimoto, K., Akagi, Y., Mawatari, M., Ueda, A., Kawakami, J., Komatsu, J., & Izumo, T. (2020). Anxiety, depression, and resilience of healthcare workers in Japan during the coronavirus disease 2019 outbreak. *Internal MedIcine*, *59*, 2693–2699.

Blanc, J., Briggs, A. Q., Seixas, A. A., Reid, M., Jean-Louis, G., & Pandi-Perumal, S. R. (2021). Addressing psychological resilience during the coronavirus disease 2019 pandemic: A rapid review.*Current Opinion in Psychiatry*, *34*, 29–35.

Brewer, W. J., Edwards, J., Anderson, V., Robinson, T., & Pantelis, C. (1996). Neuropsychological, olfactory, and hygiene deficits in men with negative symptom schizophrenia. *BiolOgical Psychiatry*, *40*, 1021–1031.

Carifio, J., & Perla, R. J. (2007). Ten common misunderstandings, misconceptions, persistent myths and urban legends about likert scales and likert response formats and their antidotes. *Journal of Social Sciences*, *3*(3), 106–116. https://doi.org/10.3844/jssp.2007.106.116

Coulombe, S., Pacheco, T., Cox, E., Khalil, C., Doucerain, M. M., Auger, E., & Meunier, S. (2020). Risk and resilience factors during the COVID-19 pandemic: A snapshot of the experiences of Canadian workers early on in the crisis. *Frontiers in Psychology*, *11*, 580702.

Dipasquale, S., Pariante, C. M., Dazzan, P., Aguglia, E., McGuire, P., & Mondelli, V. (2013). The dietary pattern of patients with schizophrenia: A systematic review. *Journal of Psychiatric Research*, *47*, 197–207.

Fiorillo, A., & Gorwood, P. (2020). The consequences of the COVID-19 pandemic on mental health and implications for clinical practice. *European Psychiatry*, *63*, e32.

Fond, G., Pauly, V., Leone, M., Llorca, P.-M., Orleans, V., Loundou, A., Lancon, C., Auquier, P., Baumstarck, K., & Boyer, L. (2021). Disparities in intensive care unit admission and mortality among patients with schizophrenia and COVID-19: A national cohort study. *Schizophrenia Bulletin*, *47*, 624–634.

García-Sierra, R., Fernández-Cano, M. I., Manresa-Domínguez, J. M., Feijoo-Cid, M., Moreno Gabriel, E., Arreciado Marañón, A., Ramos-Roure, F., Segura-Bernal, J., & Torán-Monserrat, P. (2020). Psychological distress and somatization in immigrants in primary health care practices. *Healthcare (Basel)*, *8*(4), 557. https://doi.org/10.3390/healthcare8040557

Hammarberg, K., Tran, T., Kirkman, M., & Fisher, J. (2020). Sex and age differences in clinically significant symptoms of depression and anxiety among people in Australia in the first month of COVID-19 restrictions: A national survey. *BMJ Open*, *10*, e042696.

Ito, Y., Shibata, M., Tanaka, Y., Terasawa, Y., & Umeda, S. (2019). Affective and temporal orientation of thoughts: Electrophysiological evidence. *Brain Research*, *1719*, 148–156. https://doi.org/10.1016/j.brainres.2019.05.041

Kato, M., Hori, H., Inoue, T., Iga, J., Iwata, M., Inagaki, T., Shinohara, K., Imai, H., Murata, A., Mishima, K., & Tajika, A. (2021). Discontinuation of antidepressants after remission

with antidepressant medication in major depressive disorder: A systematic review and meta-analysis. *Molecular Psychiatry*, *26*(1), 118–133.

Kavoor, A. R. (2020). COVID-19 in people with mental illness: Challenges and vulnerabilities. *Asian Journal of Psychiatry*, *51*, 102051.

Kimhi, S., Marciano, H., Eshel, Y., & Adini, B. (2020). Resilience and demographic characteristics predicting distress during the COVID-19 crisis. *Social Science & Medicine*, *265*, 113389.

Koreki, A., Nakane, J., Kitada, S., Hamaya, T., Ishii, H., Akimoto, K., Aso, K., & Onaya, M. (2020). Impact of COVID-19 on psychiatric day care services. *Asian Journal of Psychiatry*, *54*, 102442. https://doi.org/10.1016/j.ajp.2020.102442

Lee, J. H., Nam, S. K., Kim, A.-R., Kim, B., Lee, M. Y., & Lee, S. M. (2013). Resilience: A meta-analytic approach. *Journal of Counseling & Development*, *91*(3), 269–279. https://doi.org/10.1002/j.1556-6676.2013.00095.x

Lenzo, V., Quattropani, M. C., Musetti, A., Zenesini, C., Freda, M. F., Lemmo, D., Vegni, E., Borghi, L., Plazzi, G., Castelnuovo, G., Cattivelli, R., Saita, E., & Franceschini, C. (2020). Resilience contributes to low emotional impact of the COVID-19 outbreak among the general population in Italy. *Frontiers in Psychology*, *11*, 576485.

Leucht, S., Tardy, M., Komossa, K., Heres, S., Kissling, W., Salanti, G., & Davis, J. M. (2012). Antipsychotic drugs versus placebo for relapse prevention in schizophrenia: A systematic review and meta-analysis. *The Lancet*, *379*(9831), 2063–2071.

López Steinmetz, L. C., Dutto Florio, M. A., Leyes, C. A., Fong, S. B., Rigalli, A., & Godoy, J. C. (2020). Levels and predictors of depression, anxiety, and suicidal risk during COVID-19 pandemic in Argentina: The impacts of quarantine extensions on mental health state. *Psychology, Health & Medicine*, *27*(1), 13–29.

Masten, A. S. (2015). *Ordinary magic: Resilience in development*. Guilford Publications.

McGrath, P. J., Stewart, J. W., Quitkin, F. M., Chen, Y., Alpert, J. E., Nierenberg, A. A., Fava, M., Cheng, J., & Petkova, E. (2006). Predictors of relapse in a prospective study of fluoxetine treatment of major depression. *American Journal of Psychiatry*, *163*(9), 1542–1548. https://doi.org/10.1176/ajp.2006.163.9.1542

Nakajima, A., Kanie, A., Ito, M., Hirabayashi, N., Imamura, F., Takebayashi, Y., & Horikoshi, M. (2020). Cognitive behavioral therapy reduces benzodiazepine anxiolytics use in Japanese patients with mood and anxiety disorders: A retrospective observational study. *Neuropsychiatric Disease and Treatment*, *16*, 2135–2142.

O'Brien, C. P. (2005). Benzodiazepine use, abuse, and dependence. *The Journal of Clinical Psychiatry*, *66*(Suppl 2), 28–33.

Pietrzak, R. H., Feingold, J. H., Feder, A., Charney, D. S., Peccoralo, L., Southwick, S. M., & Ripp, J. (2020). Psychological resilience in frontline health care workers during the acute phase of the COVID-19 pandemic in New York City. *The Journal of Clinical Psychiatry*, *82*(1), 16115. https://doi.org/10.4088/JCP.20l13749

Pinkham, A. E., Ackerman, R. A., Depp, C. A., Harvey, P. D., & Moore, R. C. (2020). A Longitudinal nvestigation of the effects of the COVID-19 pandemic on the mental health of individuals with pre-existing severe mental illnesses. *Psychiatry Research*, *294*, 113493.

Quittkat, H. L., Düsing, R., Holtmann, F.-J., Buhlmann, U., Svaldi, J., & Vocks, S. (2020). Perceived impact of Covid-19 across different mental disorders: A study on disorder-specific symptoms, psychosocial stress and behavior. *Frontiers in Psychology*, *11*, 586246. https://doi.org/10.3389/fpsyg.2020.586246

Robinson, D., Woerner, M. G., Alvir, J. M. J., Bilder, R., Goldman, R., Geisler, S., Koreen, A., Sheitman, B., Chakos, M., Mayerhoff, D., & Lieberman, J. A. (1999). Predictors of relapse following response from a first episode of schizophrenia or schizoaffective disorder. *Archives of General Psychiatry*, *56*(3), 241–247. https://doi.org/10.1001/archpsyc.56.3.241

Scholten, W. D., Batelaan, N. M., van Balkom, A. J., Penninx, B. W., Smit, J. H., & van Oppen, P. (2013). Recurrence of anxiety disorders and its predictors. *Journal of Affective Disorders*, *147*(1–3), 180–185. https://doi.org/10.1016/j.jad.2012.10.031

Suzuki, T., Uchida, H., Takeuchi, H., Tsuboi, T., Hirano, J., & Mimura, M. (2014). A review on schizophrenia and relapse-a quest for user-friendly psychopharmacotherapy. *Human Psychopharmacology: Clinical and Experimental*, *29*(5), 414–426. https://doi.org/10.1002/hup.2421

Ungar, M., & Theron, L. (2020). Resilience and mental health: How multisystemic processes contribute to positive outcomes. *Lancet Psychiatry*, *7*, 441–448.

Varma, P., Junge, M., Meaklim, H., & Jackson, M. L. (2021). Younger people are more vulnerable to stress, anxiety and depression during COVID-19 pandemic: A global cross-sectional survey. *Progress in Neuro-Psychopharmacology and Biological Psychiatry*, *109*, 110236.

Vázquez, G. H., Holtzman, J. N., Lolich, M., Ketter, T. A., & Baldessarini, R. J.(2015). Recurrence rates in bipolar disorder: Systematic comparison of long-term prospective, naturalistic studies versus randomized controlled trials. *European Neuropsychopharmacology*, *25*(10), 1501–1512.

Wang, Q., Xu, R., & Volkow, N. D. (2021). Increased risk of COVID-19 infection and mortality in people with mental disorders: Analysis from electronic health records in the United States. *World Psychiatry*, *20*, 124–130.

World Health Organization (2004). *The international statistical classification of diseases and health related problems ICD-10: Tenth revision. Volume 2: Instruction manual*. Author.

Wu, T., Jia, X., Shi, H., Niu, J., Yin, X., Xie, J., & Wang, X. (2021). Prevalence of mental health problems during the COVID-19 pandemic: A systematic review and meta-analysis. *Journal of Affective Disorders*, *281*, 91–98. https://doi.org/10.1016/j.jad.2020.11.117