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Are Patients with Mental Disorders More Vulnerable to Loneliness and Social Isolation During the COVID-19 Pandemic? – Findings from the Japan COVID-19 and Society Internet Survey

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ABSTRACT

Background: Loneliness and social isolation are well-known factors that worsen the symptoms among patients with mental disorders. Few previous studies have explored loneliness and social isolation among populations with mental disorders during the coronavirus disease 2019 (COVID-19) pandemic. Therefore, our study examined the mental health impact of the pandemic on these population groups in terms of loneliness and social isolation.

Methods: We used data from the Japan COVID-19 and Society Internet Surveys, a large-scale online survey. Using multivariable logistic regression analysis, we calculated the odds ratios and 95% confidence intervals (CIs) of moderate-to-severe loneliness and high social isolation for major chronic diseases, including mental disorders, after adjusting for potential confounders. Calculations were performed for each type of mental disorder. Finally, calculations were performed to explore the association between moderate-to-severe loneliness or high social isolation and psychiatric symptoms among patients with mental disorders.

Results: Of the 28175 participants, 2021 (7.2%) had a mental disorder. Mental disorders, especially depression and anxiety disorders, were found to be associated with a higher risk of moderate-to-severe loneliness and high social isolation. Patients with mental disorders who experienced moderate-to-severe loneliness and high social isolation were found to have exacerbated psychiatric symptoms.

Limitation: Our findings were obtained from a cross-sectional study design.

Conclusions: Patients with mental disorders were more vulnerable to moderate-to-severe loneliness and high social isolation during the pandemic, which contributed to the exacerbation of their symptoms. Depression and anxiety, in particular, were most likely to occur and required special attention.

Keywords: Mental disorders, Loneliness, Social isolation, COVID-19 pandemic, Depression, Anxiety

1. INTRODUCTION

Loneliness and social isolation are well-known factors that contribute to increased morbidity and mortality (Cacioppo and Cacioppo, 2018). While loneliness refers to a subjective condition of feeling disconnected, even among the company of other people, social isolation describes the actual lack of social connections. Both these concepts are related but inherently different (Tomaka et al., 2006). Loneliness and social isolation have been found to increase the risk of cardiovascular diseases (Holt-Lunstad and Smith, 2016), chronic physical conditions such as obesity and diabetes (Ida et al., 2020; Nonogaki et al., 2007; Petitte et al., 2015), impaired cognitive ability (Ong et al., 2016; Shen et al., 2022), and mental health issues (Hawkey and Cacioppo, 2010). Patients with mental disorders, in particular, have been

reported to experience worsening of their symptoms (Prince et al., 2018), and even higher suicide rates (Stravynski and Boyer, 2001), as a result of loneliness and social isolation.

The novel coronavirus disease 2019 (COVID-19) pandemic, which started on March 11, 2020 (World Health Organization, n.d.), has greatly impacted people worldwide, whether economically, socially, or in terms of health and psychological factors (Shamasunder et al., 2020). Experts have warned about the pervasive effects of the pandemic on the mental health of the general population (Najam, 2020), and several studies have noted that more people experienced higher levels of psychological distress (Xiong et al., 2020), loneliness (Hwang et al., 2020), and suicidality (Bell et al., 2021) during the pandemic than during pre-pandemic times. Social distancing, quarantine, and lockdown measures have been identified as the main factors leading to this phenomenon (Brooks et al., 2020; Chinna et al., 2021; Matias et al., 2020).

Although the mental health effects of the pandemic on the general population have been well explored, its ramifications for people with mental disorders have been discussed less frequently (Hossain et al., 2020). In particular, relatively few studies have reported on loneliness and social isolation among populations with mental disorders during the pandemic (Burrai et al., 2020; Heron et al., 2022; Lee et al., 2022). These studies also tended to have limited sample sizes or the samples were not representative of various mental disorders; therefore, there is a need for large, population-based studies.

Our study aimed to examine the impact of the pandemic on individuals with mental disorders using a large representative sample. First, we compared the risk of loneliness and social isolation during the pandemic between individuals with and without mental disorders. Second, we examined the relationships between various types of mental disorders, loneliness, and social isolation. Finally, we explored the potential consequences of loneliness and social isolation in terms of moderate or serious mental distress, suicidal ideation, and the exacerbation of psychiatric symptoms.

We used data from the Japan COVID-19 and Society Internet Survey (JACSIS), a population-based survey conducted during the pandemic. Our goal was that the findings of this study could be applied to better inform strategies to identify and support vulnerable subgroups of the population as the pandemic continues or in future pandemics.

2. METHODS

2.1. Study design and population

This study used online survey data collected from JACSIS. The JACSIS is a web-based, self-report questionnaire survey conducted by the Internet research firm, Rakuten Insight. Related surveys, using a similar approach, have been conducted multiple times since 2015. This study was approved by the Research Ethics Committee of the Osaka International

Cancer Institute (approved June 19, 2020; Approval No. 20084) and the Ethics Committee of the Obihiro Daiichi Hospital (approved November 10, 2022; Approval No. not applicable).

This study used data from 31000 Japanese participants, aged 18 to 79 years, who participated in the September-October 2021 survey. This pool of participants included 22838 participants, randomly selected from another pool of 33081 participants who participated in previous surveys, as well as 8162 panel members, newly registered at the end of October 2021. Of the 31000 total participants in the study, 28175 participants were included in the final analysis, after excluding 2825 participants judged to have made unnatural or other responses.

2.2. Measurements

2.2.1. Loneliness

The Japanese version of the three-item University of California, Los Angeles (UCLA) Loneliness Scale (UCLA-LS3-SF3) was used to measure loneliness (Arimoto and Tadaka, 2019; Hughes et al., 2004). This is a shortened version of the 20-item revised UCLA Loneliness Scale, which assesses three items (the lack of companionship, feeling left out, and isolation from others). In the original version, the items are rated on a four-point scale: 1 (never), 2 (rarely), 3 (sometimes), and 4 (always). The total UCLA-LS3-SF3 score ranges from 3 to 12, with higher scores indicating more severe loneliness. The original methodology

for this survey was modified based on a previous report. In the modified version, the three items were answered on a five-point scale: 1 (never), 2 (rare), 3 (sometimes), 4 (often), and 5 (always). The total score ranged from 3 to 15. Therefore, a tertile was set up in this study, similar to previous reports. The third tertile, with a total score of 6 or above, was defined as “moderate-to-severe loneliness” (Yamada et al., 2021).

2.2.2. Social isolation

The Japanese version of the 6-item Lubben Social Network Scale (LSNS-6) was used to measure social isolation (Kurimoto et al., 2011; Lubben, n.d.; Lubben et al., 2006). The following six questions were asked: 1) “How many relatives do you see or hear from at least once a month?”; 2) “How many relatives do you feel close to such that you could call on them for help?”; 3) “How many relatives do you feel at ease with that you can talk about private matters?”; 4) “How many of your friends do you see or hear from at least once a month?”; 5) “How many friends do you feel close to such that you could call on them for help?”; 6) “How many friends do you feel at ease with that you can talk about private matters?” The LSNS-6 is answered on a six-point scale: 0 (none), 1 (one), 2 (two), 3 (three or four), 4 (five to eight), and 5 (nine or more). The total score ranges from 0 to 30, with higher scores indicating greater social engagement. In this study, participants who scored less than 12 points were defined as having high social isolation, as reported previously (Lubben et al., 2006).

2.2.3. Psychological distress

Psychological distress was assessed using the Kessler Psychological Distress Scale (K6). The K6 consists of six questions, and each item is answered on a five-point scale: 0 (never), 1 (rarely), 2 (sometimes), 3 (often), or 4 (always). The total score ranged from 0 to 24, with a score ≥ 13 indicating severe psychological distress (Prochaska et al., 2012).

2.2.4. Suicidal ideation

Suicidal ideation was assessed using the question: “In the last two months, have you had thoughts in which you wished you were dead?” The answers to the question were: 1) “I experienced it for the first time in the last two months”; 2) “I have experienced it before, and I still experience it now”; 3) “I have experienced it before, but not now”; 4) “I have never experienced it.” In this study, participants who answered 1) or 2) were defined as having suicidal ideation.

2.2.5. Exacerbation of psychiatric symptoms

Regarding the exacerbation of psychiatric symptoms, participants were asked the following question: “Have your psychiatric symptoms or medical condition worsened in the last two months?” Participants who answered “yes” were considered to have experienced an exacerbation of psychiatric symptoms.

2.2.6. Demographic characteristics

Demographic variables included sex, age (<40, 40–60, >60 years), occupation classification (unemployed, self-employed, nonregular employee, regular employee), number

of household members (1, 2, >2), absence/presence of spouse (no/yes), having children (no/yes), annual household income (<2, 2–6, >6 million yen, no response or unknown), education level (high school educated or lower, college educated or higher, other), alcohol use (never, ever, current), smoking status (never, ever, current), COVID-19 infection status in residential areas (lowest, second, third, and highest quartiles), and absence/presence of disease (no/yes). The area of residence for each COVID-19 infection status was defined by dividing the number of patients per million in each prefecture into quartiles between January 16, 2020, when the COVID-19 infection was first confirmed in Japan, and October 31, 2021, the end date of this study. The term “chronic diseases” focused on five diseases (diabetes, myocardial infarction, stroke, cancer, and mental disorders) that the Japanese Ministry of Health, Labour, and Welfare has identified as requiring expansive and continuous medical care. In our study, we further investigated the presence of the following mental disorders: dementia, schizophrenia, bipolar disorder, depression, anxiety disorder, obsessive-compulsive disorder, and eating disorder. Duplication was permitted for the presence of each mental disorder.

2.3. Management of the data quality

To identify participants who provided unnatural responses, we analyzed their responses to the following three questions: (1) “Please select the second to last option from the following options”; (2) “Do you currently drink or use alcohol or drugs?”; (3) “Do you currently have a pre-existing medical condition?” To maintain the data quality, participants

who provided inconsistent or unnatural responses to these questions were excluded. Excluded participants included participants who did not select the correct option (did not select the second to last option) on question (1), those who answered positively to all questions about drugs (marijuana, cocaine, heroin, etc.) in question (2), and those who answered positively to all questions regarding the given diseases in question (3).

2.4. Statistical analyses

In this study, multivariable logistic regression analysis was used to examine the association between loneliness, social isolation, and chronic diseases (diabetes, myocardial infarction and angina, stroke, cancer, and mental disorders) after adjusting for demographic variables. Furthermore, we examined the association between each mental disorder and loneliness or social isolation by replacing the presence or absence of mental disorders with the presence or absence of dementia, schizophrenia, bipolar disorder, depression, anxiety disorder, obsessive-compulsive disorder, or eating disorders. To examine the association of loneliness and social isolation with mental distress, suicidal ideation, and the exacerbation of psychiatric symptoms for each mental disorder, we stratified the patients by the type of mental disorder, added the presence of moderate and severe loneliness and high social isolation as explanatory variables, and then conducted logistic analyses with the objective variables of mental distress, suicidal ideation, and the exacerbation of psychiatric symptoms, adjusted for demographic variables, except for the presence or absence of chronic diseases.

The odds ratios (OR) and 95% confidence intervals (CI) were calculated using multivariable logistic regression analysis, based on the reference group set for each variable. All statistical analyses were performed using the dplyr package in R statistics 4.0.2.

3. RESULTS

3.1. Participant characteristics

Table 1 presents the participants' characteristics. Of the 28175 participants, 2021 (7.2%) had a mental disorder, including dementia (0.4%), schizophrenia (0.9%), bipolar disorder (1.4%), depression (4.0%), anxiety disorder (2.5%), obsessive-compulsive disorder (1.7%), and eating disorders (0.9%). Of those with a mental disorder, 65.1% reported having more than one mental disorder. Of all the participants, 53.6% had moderate-to-severe loneliness (UCLA-LS3-SF3 ≥ 6) and 57.0% had high social isolation (LSNS-6 < 12).

3.2. Association between loneliness, social isolation and mental disorders during the COVID-19 pandemic

We examined the association between five major diseases (diabetes, myocardial infarction and angina, stroke, cancer, and mental disorders) and loneliness or social isolation during the COVID-19 pandemic using multivariable logistic regression analysis after adjusting for demographic variables. The results showed that patients with myocardial

infarction (OR = 1.22, 95% CI = 1.03–1.45), stroke (OR = 1.29, 95% CI = 1.01–1.63), and mental disorders (OR = 3.67, 95% CI = 3.25–4.14) had a significantly higher risk of moderate-to-severe loneliness, and only mental disorders (OR = 2.01, 95% CI = 1.80–2.25) had a significantly higher risk of social isolation (Table 2). Further detailed examination of mental disorders showed that dementia (OR = 0.44, 95% CI = 0.23–0.87) was associated with a significantly lower risk of moderate-to-severe loneliness, while depression (OR = 2.78, 95% CI = 2.31–3.35) and anxiety disorders (OR = 2.32, 95% CI = 1.80–2.98) were associated with a significantly higher risk of moderate-to-severe loneliness (Table 3). With regard to social isolation, individuals with depression (OR = 1.99, 95% CI = 1.68–2.37) or anxiety disorders (OR = 1.27, 95% CI = 1.02–1.57) were at a significantly higher risk (Table 3).

3.3. Impact of loneliness and social isolation on psychiatric symptoms in patients with mental disorders.

We examined the impact of loneliness and social isolation on psychiatric symptoms in patients with mental disorders. Table 4 presents the results of the impact of moderate-to-severe loneliness on psychiatric symptoms in patients with mental disorders. For mental disorders, moderate-to-severe loneliness increased mental distress (OR = 13.39, 95% CI = 8.20–21.88), suicidal ideation (OR = 2.90, 95% CI = 1.49–5.66), and the risk of exacerbation of psychiatric symptoms (OR = 2.66, 95% CI = 1.83–3.88). When examined by disease, the

results showed that moderate-to-severe loneliness increased psychological distress in all mental disorders except for dementia. Suicidal ideation was increased in patients with depression (OR = 3.42, 95% CI = 1.30–8.98) who were moderately or severely lonely. Furthermore, patients with schizophrenia (OR = 2.91, 95% CI = 1.09–7.79), depression (OR = 2.79, 95% CI = 1.68–4.63), and anxiety disorders (OR = 2.07, 95% CI = 1.17–3.69) who had moderate-to-severe loneliness were associated with an increased risk of exacerbation of psychiatric symptoms.

The impact of high social isolation on psychiatric symptoms in patients with mental disorders is shown in Table 5. Patients with mental disorders and high social isolation were shown to have significantly increased psychological distress (OR = 1.56, 95% CI = 1.22–2.00). Among mental disorders, depression (OR = 1.79, 95% CI = 1.27–2.53) and anxiety disorders (OR = 1.65, 95% CI = 1.12–2.44) showed that high social isolation was associated with higher psychological distress. Furthermore, an increased risk of exacerbation of psychiatric symptoms was shown in patients with dementia (OR = 3.13, 95% CI = 1.03–9.54), schizophrenia (OR = 2.52, 95% CI = 1.21–5.24), bipolar disorder (OR = 2.48, 95% CI = 1.38–4.45), depression (OR = 1.50, 95% CI = 1.04–2.18), and obsessive-compulsive disorder (OR = 2.02, 95% CI = 1.05–3.88), who are at higher risk of social isolation. In contrast, no association was found between suicidal ideation and social isolation for any mental disorder.

4. DISCUSSION

The study results revealed three significant findings. First, the presence of a mental disorder was associated with a higher risk of moderate-to-severe loneliness and higher social isolation during the COVID-19 pandemic, after adjusting for potential confounders. Second, when analyzed according to the type of mental disorder, depressive and anxiety disorders were associated with a significantly higher risk of moderate-to-severe loneliness and higher social isolation during the COVID-19 pandemic. However, dementia was associated with a significantly lower risk of moderate-to-severe loneliness. Finally, moderate-to-severe loneliness was associated with a significantly higher risk of serious psychological distress, suicidal ideation, and exacerbation of psychiatric symptoms, whereas high social isolation was associated with a higher risk of serious psychological distress and exacerbation of psychiatric symptoms.

Our first finding, that patients with mental disorders were exposed to a higher risk of moderate-to-severe loneliness and higher social isolation during the COVID-19 pandemic than those without mental disorders, is important in several ways. Whereas previous studies have mostly focused on smaller sample sizes, for example, Heron et al. (2022) with $n=367$ and Burrai et al. (2020) with $n=82$, or on samples controlled for a single demographic variable, such as age (Gilsbach et al., 2021), this study used data from a large-scale ($n=28175$), nationwide population sample representative of the major demographic variables,

including age, sex, residential location, and household income. We believe that we benefited from the large population sample, as it provided a more reliable degree of power for statistical analysis. Furthermore, the representation provided by the data indicates that mental disorders are a significant factor in determining the risk of loneliness or social isolation during a pandemic. This is a relevant and novel finding that contributes to the current literature.

There are several possible reasons why patients with mental disorders are more prone to a higher risk of moderate-to-severe loneliness and higher social isolation during the COVID-19 pandemic. One reason may be that the pandemic prevented access to critical social support services that patients with mental disorders would have received during normal times (Choi et al., 2020). Lockdowns and quarantines (Benke et al., 2020), the closure of public places such as schools (Lee, 2020), and work-from-home policies may have acted as additional environmental barriers for these patients to interact with other individuals. Our results highlight the urgency of, and reinforce the need for, better strategies to identify patients with mental disorders, who are at a more unfavorable disposition during the pandemic, as well as the provision of more adequate social support and services by the relevant authorities to alleviate these patients' concerns.

Based on our extensive literature review, to the best of our knowledge, this is the first study to investigate how various mental disorders can be affected by COVID-19. Our results indicated that patients with depressive and anxiety disorders are more vulnerable to the

effects of the pandemic in terms of the development of moderate-to-severe loneliness and high social isolation than those with other types of mental disorders. Beutel et al. (2017) and Saris et al. (2017) found that during non-pandemic times, depressive and anxiety disorders were closely linked to higher levels of loneliness and impaired social functioning. While questions regarding the underlying pathophysiology remain largely elusive, Saris et al. offered a plausible explanation in which social interactions may be perceived as less fulfilling by patients with depressive and anxiety disorders due to the underlying impairment of the brain's reward system (Saris et al., 2017). We deduce that this was also true during the pandemic. Environmental barriers during the pandemic, such as the lockdown mentioned earlier, would have further alienated patients with depressive or anxiety disorders from other individuals. Both internal and external factors seem to have contributed to the adverse psychological impact of the pandemic on these patients.

Interestingly, dementia was associated with a significantly lower risk of moderate-to-severe loneliness during the COVID-19 pandemic. Before the pandemic, the association between dementia and loneliness was largely inconclusive, owing to variations in methodologies among studies (Victor, 2021). In a study of 1176 older adults, Lampinen et al. (2022) found no significant differences in loneliness between participants with and without dementia. In our case, we believe that the reduction in the risk of loneliness could be attributed to an increase in the proportion of caregivers for individuals with dementia (usually

healthy adults), who had to stay at home more often due to the outbreak. Despite the increased caregiver burden during the pandemic, as highlighted by Otobe et al. (2022), the longer time spent at home by caregivers may have had an unexpected benefit of increasing the level of social support received by patients with dementia, thereby alleviating feelings of disconnection (Victor et al., 2020). While we do not suggest that caregivers should stay at home more, regardless of their other commitments, we encourage governments to consider proposals to enhance the support provided to home caregivers of patients with dementia, including financial subsidies (Costa-Font and Vilaplana-Prieto, 2022) and empowerment programs (Yoon and Kim, 2020).

This study also investigated the relationships between loneliness, social isolation, and psychiatric symptoms among patients with mental disorders. The results indicated that patients with mental disorders suffering from moderate-to-severe loneliness or high social isolation were at a higher level of susceptibility to exacerbation of psychiatric symptoms and serious psychological distress. All these factors could result in more time and medical resources being required for the treatment of these individuals (Grabe et al., 2009; Chiu et al., 2017; Luppá et al., 2012).

These results also suggest that suicidal ideation is associated with loneliness among patients with mental disorders. This poses many challenges to society regarding the additional clinical and economic costs of treatment (Neslusan et al., 2022), as well as the reduction in

the overall quality of life (Alves et al., 2016). Therefore, timely and effective strategies for managing social disconnection and feelings of loneliness among patients with mental disorders are strongly recommended.

4.1 Limitations

Despite the significance of the results discussed above, this study had several limitations. First, because the data were drawn from a population-based survey conducted online, there could have been some sampling bias, as those without access to the Internet could be underrepresented. However, a survey conducted by the Ministry of Internal Affairs and Communications in 2021 (Ministry of Internal Affairs and Communications, 2022) indicated that the Internet penetration rate in Japan was 82.9%. Therefore, we infer that the possibility of sample bias is small because the number of people in Japan who do not have access to the Internet is low. Furthermore, the survey was conducted using a self-reported questionnaire; therefore, the data collected regarding medical history may not have been fully accurate. This is especially true for mental disorders that are not always diagnosed according to operational diagnostic criteria, such as the DSM-5. Thus, the data would not properly reflect the actual conditions of the participants. Nevertheless, we found that the prevalence of each type of mental disorder in our survey population was similar to the results of other large-scale, population-based surveys conducted in Japan, such as the World Mental Health Japan

Survey (Ishikawa et al., 2016, Supplementary Table). Hence, it can be concluded that our findings have not been largely compromised. Finally, as this was a cross-sectional study, it was not possible to track the changes in the levels of loneliness and social isolation, as well as the psychological impacts on individuals over time. Further research is warranted to study the longitudinal course of the pandemic.

5. CONCLUSION

The results of our study indicate that patients with mental disorders are more vulnerable to a higher risk of moderate-to-severe loneliness and higher social isolation during the COVID-19 pandemic. Patients with depressive and anxiety disorders are particularly affected, highlighting the need for special attention. Moderate-to-severe loneliness and high social isolation are associated with a higher risk of serious psychological distress, suicidal ideation, and exacerbation of psychiatric symptoms among patients.

On May 5, 2023, the World Health Organization announced that the COVID-19 pandemic “no longer fit the definition of a Public Health Emergency of International Concern (PHEIC)” (World Health Organization Europe, 2023). Nevertheless, it is crucial to plan for future pandemics since we live in an age of ever-increasing uncertainty. We believe that the findings of this study can be used to inform local and national governments about the need to

identify vulnerable groups within the population during pandemics, especially those with specific mental disorders, and devise strategies to alleviate their concerns.

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386 **AUTHOR CONTRIBUTIONS**

387 Keng Wee GOH: Formal analysis, Investigation, Writing-Original Draft

388 Shuhei Ishikawa: Conceptualization, Investigation, Writing-Original Draft

389 Ryo Okubo: Conceptualization, Project administration, Investigation, Supervision,

390 Methodology

391 Ichiro Kusumi: Investigation, Supervision

392 Takahiro Tabuchi: Conceptualization, Project administration, Investigation, Supervision,

393 Methodology, Funding acquisition

394

AUTHOR STATEMENT

All authors have read and approved the contents of the submitted manuscript. All authors have agreed to be listed as co-authors and accepted the order of authorship. This manuscript has not been published previously and is not under consideration for publication elsewhere.

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634 **Table 1. Participant characteristics**

	Values									
	Total (n=28175)		Loneliness				Social isolation			
			No to mild (n=13075)		Moderate-to-severe (n=15100)		Low (n=12108)		High (n=16067)	
Sex, n (%)										
Male	14305	(50.8)	6290	(48.1)	8015	(53.1)	6609	(54.6)	7696	(47.9)
Age, n (%)										
Younger (<40 years)	8348	(29.6)	3651	(27.9)	4697	(31.1)	3917	(32.4)	4431	(27.6)
Middle-aged (40–60 years)	12473	(44.3)	5350	(40.9)	7123	(47.2)	4455	(36.8)	8018	(49.9)
Elder (>60 years)	7354	(26.1)	4074	(31.2)	3280	(21.7)	3736	(30.9)	3618	(22.5)
Occupation classification, n (%)										
Unemployed	9858	(35.0)	4552	(34.8)	5306	(35.1)	4270	(35.3)	5588	(34.8)
Self-employed	1904	(6.8)	922	(7.1)	982	(6.5)	823	(6.8)	1081	(6.7)
Non-regular employee	5701	(20.2)	2527	(19.3)	3174	(21.0)	2490	(20.6)	3211	(20.0)
Regular employee	10712	(38.0)	5074	(38.8)	5638	(37.3)	4525	(37.4)	6187	(38.5)
Number of household members, n (%)										
1	5910	(21.0)	2384	(18.2)	3526	(23.4)	2121	(17.5)	3789	(23.6)
2	9699	(34.4)	4781	(36.6)	4918	(32.6)	4042	(33.4)	5657	(35.2)
>2	12566	(44.6)	5910	(45.2)	6656	(44.1)	5945	(49.1)	6621	(41.2)
Spouse, yes: n (%)	16969	(60.2)	8598	(65.8)	8371	(55.4)	7811	(64.5)	9158	(57.0)
Having children, yes: n (%)										
Annual household income, n (%)										
< 2 million yen	2415	(8.6)	863	(6.6)	1552	(10.3)	725	(6.0)	1690	(10.5)
2-6 million yen	11091	(39.4)	5097	(39.0)	5994	(39.7)	4617	(38.1)	6474	(40.3)
> 6 million yen	8621	(30.6)	4339	(33.2)	4282	(28.4)	4185	(34.6)	4436	(27.6)
No response/unknown	6048	(21.5)	2776	(21.2)	3272	(21.7)	2581	(21.3)	3467	(21.6)
Educational level, n (%)										
High school educated or lower	7984	(28.3)	3656	(28.0)	4328	(28.7)	3296	(27.2)	4688	(29.2)
College educated or higher	20025	(71.1)	9348	(71.5)	10677	(70.7)	8763	(72.4)	11262	(70.1)
Other	166	(0.6)	71	(0.5)	95	(0.6)	49	(0.4)	117	(0.7)
Alcohol use, n (%)										
Never	11429	(40.6)	5143	(39.3)	6286	(41.6)	4695	(38.8)	6734	(41.9)
Ever	2150	(7.6)	825	(6.3)	1325	(8.8)	859	(7.1)	1291	(8.0)
Current	14596	(51.8)	7107	(54.4)	7489	(49.6)	6554	(54.1)	8042	(50.1)

Smoking status, n (%)									
Never	17534	(62.2)	8180	(62.6)	9354	(61.9)	7769	(64.2)	9765 (60.8)
Ever	5477	(19.4)	2602	(19.9)	2875	(19.0)	2220	(18.3)	3257 (20.3)
Current	5164	(18.3)	2293	(17.5)	2871	(19.0)	2119	(17.5)	3045 (19.0)
COVID-19 infection status in residential areas, n (%)									
Lowest quartiles	2915	(10.3)	1377	(10.5)	1538	(10.2)	1274	(10.5)	1641 (10.2)
Second quartiles	2902	(10.3)	1295	(9.9)	1607	(10.6)	1253	(10.3)	1649 (10.3)
Third quartiles	4917	(17.5)	2237	(17.1)	2680	(17.7)	2150	(17.8)	2767 (17.2)
Highest quartiles	17441	(61.9)	8166	(62.5)	9275	(61.4)	7431	(61.4)	10010 (62.3)
Diseases, yes: n (%)									
Diabetes	1999	(7.1)	932	(7.1)	1067	(7.1)	851	(7.0)	1148 (7.1)
Myocardial infarction and angina	724	(2.6)	267	(2.0)	457	(3.0)	323	(2.7)	401 (2.5)
Stroke	426	(1.5)	122	(0.9)	304	(2.0)	180	(1.5)	246 (1.5)
Cancer	685	(2.4)	263	(2.0)	422	(2.8)	294	(2.4)	391 (2.4)
Mental disorders	2021	(7.2)	346	(2.6)	1675	(11.1)	532	(4.4)	1489 (9.3)
Dementia	124	(0.4)	21	(0.2)	103	(0.7)	50	(0.4)	74 (0.5)
Schizophrenia	267	(0.9)	45	(0.3)	222	(1.5)	83	(0.7)	184 (1.1)
Bipolar disorder	381	(1.4)	69	(0.5)	312	(2.1)	120	(1.0)	261 (1.6)
Depression	1124	(4.0)	177	(1.4)	947	(6.3)	270	(2.2)	854 (5.3)
Anxiety disorder	703	(2.5)	98	(0.7)	605	(4.0)	197	(1.6)	506 (3.1)
Obsessive-compulsive disorder	277	(1.0)	41	(0.3)	236	(1.6)	93	(0.8)	184 (1.1)
Eating disorder	244	(0.9)	36	(0.3)	208	(1.4)	87	(0.7)	157 (1.0)

635

636 Note: Loneliness was defined as moderate-to-severe loneliness for participants with UCLA-

637 LS3-SF3 scores ≥ 6 . Social isolation was defined as a high risk of social isolation for

638 participants with LSNS-6 scores of less than 12 points.

639 **Table 2. Association between participant characteristics and loneliness or social isolation**

	Moderate-to-severe loneliness			High social isolation		
	OR	(95% CI)		OR	(95% CI)	
Sex, reference: male	1.21	(1.14	- 1.28)	0.66	(0.62	- 0.70)
Age						
Younger (15-39)	0.88	(0.83	- 0.94)	0.58	(0.54	- 0.62)
Middle-aged (40-64)	reference			reference		
Older (65-79)	0.54	(0.50	- 0.58)	0.41	(0.38	- 0.45)
Occupation classification						
Unemployed	reference			reference		
Self-employed	0.76	(0.68	- 0.85)	0.75	(0.67	- 0.83)
Non-regular employee	0.82	(0.76	- 0.88)	0.82	(0.76	- 0.88)
Regular employee	0.78	(0.72	- 0.84)	0.81	(0.75	- 0.87)
Number of household members						
1	reference			reference		
2	0.94	(0.86	- 1.03)	1.06	(0.97	- 1.16)
≥ 3	1.01	(0.93	- 1.11)	0.72	(0.66	- 0.79)
Spouse, reference: no	0.79	(0.73	- 0.85)	0.81	(0.75	- 0.87)
Having children, reference: no	0.88	(0.81	- 0.96)	1.08	(0.99	- 1.17)
Annual household income						
< 2 million yen	1.19	(1.08	- 1.32)	1.41	(1.28	- 1.56)
2-6 million yen	reference			reference		
> 6 million yen	0.83	(0.78	- 0.88)	0.73	(0.69	- 0.78)
No response/unknown	0.89	(0.83	- 0.95)	0.93	(0.87	- 1.00)
Educational level						
High school educated or lower	reference			reference		
College educated or higher	1.00	(0.95	- 1.06)	0.91	(0.86	- 0.97)
Other	0.90	(0.64	- 1.24)	1.47	(1.04	- 2.08)
Alcohol use						
Never	reference			reference		
Ever	1.28	(1.16	- 1.41)	0.98	(0.89	- 1.09)
Current	0.96	(0.91	- 1.01)	0.82	(0.78	- 0.86)
Smoking status						
Never	reference			reference		
Ever	1.15	(1.08	- 1.23)	1.11	(1.03	- 1.18)
Current	1.10	(1.02	- 1.18)	0.94	(0.87	- 1.00)

COVID-19 infection status

	reference			reference		
Lowest quartiles						
Second quartiles	1.10	(0.99 - 1.23)		1.00	(0.90 - 1.11)	
Third quartiles	1.07	(0.97 - 1.17)		0.99	(0.90 - 1.09)	
Highest quartiles	1.01	(0.93 - 1.09)		1.06	(0.98 - 1.15)	
Diseases, reference: no						
Diabetes	1.00	(0.90 - 1.10)		0.96	(0.87 - 1.07)	
Myocardial infarction	1.22	(1.03 - 1.45)		0.82	(0.70 - 0.97)	
Stroke	1.29	(1.01 - 1.63)		0.79	(0.63 - 0.99)	
Cancer	1.07	(0.90 - 1.27)		0.96	(0.81 - 1.13)	
Mental disorders	3.67	(3.25 - 4.14)		2.01	(1.80 - 2.25)	

640

641 Abbreviations: OR, odds ratio; CI, confidence interval.

642

Table 3. Association between mental disorders and loneliness or social isolation.

	Moderate-to-severe loneliness		High social isolation	
	OR	(95% CI)	OR	(95% CI)
Mental disorders, reference: no				
Dementia	0.44	(0.23 - 0.87)	0.76	(0.45 - 1.30)
Schizophrenia	1.30	(0.87 - 1.93)	1.17	(0.82 - 1.66)
Bipolar disorder	1.02	(0.74 - 1.41)	0.93	(0.70 - 1.24)
Depression	2.78	(2.31 - 3.35)	1.99	(1.68 - 2.37)
Anxiety disorder	2.32	(1.80 - 2.98)	1.27	(1.02 - 1.57)
Obsessive-compulsive disorder	1.12	(0.73 - 1.72)	0.87	(0.61 - 1.23)
Eating disorder	1.27	(0.81 - 1.98)	0.83	(0.58 - 1.18)

644

645 Abbreviations: OR, odds ratio; CI, confidence interval.

646 Table 4. The impact of loneliness on psychiatric symptoms in patients with mental disorders.

	Serious psychological distress		Suicidal ideation		Exacerbation of psychiatric symptoms	
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)
Moderate-to-severe loneliness, reference: no to mild loneliness						
Mental disorders	13.4	(8.20 - 21.9)	2.90	(1.49 - 5.66)	2.66	(1.83 - 3.88)
Dementia	5.28	(0.90 - 31.1)	0.30	(0.01 - 8.76)	3.40	(0.69 - 16.8)
Schizophrenia	9.23	(2.99 - 28.5)	4.23	(0.78 - 23.0)	2.91	(1.09 - 7.79)
Bipolar disorder	6.11	(2.70 - 13.8)	2.68	(0.84 - 8.56)	1.68	(0.84 - 3.35)
Depression	10.4	(5.70 - 18.9)	3.42	(1.30 - 8.98)	2.79	(1.68 - 4.63)
Anxiety disorder	10.0	(4.85 - 20.8)	1.83	(0.68 - 4.87)	2.07	(1.17 - 3.69)
Obsessive-compulsive disorder	9.07	(3.23 - 25.5)	1.81	(0.39 - 8.32)	2.44	(0.99 - 6.02)
Eating disorder	3.16	(1.23 - 8.08)	1.52	(0.29 - 8.07)	1.99	(0.77 - 5.19)

647

648 Abbreviations: OR, odds ratio; CI, confidence interval.

Table 5. The impact of social isolation on psychiatric symptoms in patients with mental disorders.

	Serious psychological distress		Suicidal ideation		Exacerbation of psychiatric symptoms	
	OR	(95%CI)	OR	(95%CI)	OR	(95%CI)
High social isolation, reference: low social isolation						
Mental disorders	1.56	(1.22 - 2.00)	1.20	(0.77 - 1.87)	1.30	(1.00 - 1.70)
Dementia	0.47	(0.14 - 1.54)	0.27	(0.03 - 2.94)	3.13	(1.03 - 9.54)
Schizophrenia	1.33	(0.67 - 2.63)	0.59	(0.21 - 1.61)	2.52	(1.21 - 5.24)
Bipolar disorder	1.56	(0.92 - 2.66)	0.84	(0.37 - 1.92)	2.48	(1.38 - 4.45)
Depression	1.79	(1.27 - 2.53)	0.81	(0.44 - 1.48)	1.50	(1.04 - 2.18)
Anxiety disorder	1.65	(1.12 - 2.44)	0.90	(0.47 - 1.73)	1.25	(0.84 - 1.87)
Obsessive-compulsive disorder	1.53	(0.81 - 2.90)	0.72	(0.23 - 2.25)	2.02	(1.05 - 3.88)
Eating disorder	1.82	(0.95 - 3.49)	0.44	(0.14 - 1.34)	1.66	(0.85 - 3.25)

651

652 Abbreviations: OR, odds ratio; CI, confidence interval.