

Loneliness, social isolation, and pain following the COVID-19 outbreak: data from a nationwide internet survey in Japan

Keiko Yamada (✉ keiko-yamada@umin.org)

McGill University

Kenta Wakaizumi

Keio University School of Medicine

Yasuhiko Kubota

Osaka Center for Cancer and Cardiovascular Diseases Prevention

Hiroshi Murayama

Tokyo Metropolitan Institute of Gerontology

Takahiro Tabuchi

Cancer Control Center, Osaka International Cancer Institute

Research Article

Keywords: Loneliness, Social isolation, Pain, Chronic pain, COVID-19.

Posted Date: March 17th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-240504/v1>

License: © ⓘ This work is licensed under a Creative Commons Attribution 4.0 International License. [Read Full License](#)

Abstract

The aim of cross-sectional study was to investigate the association between pain and loneliness and increased social isolation during the COVID-19 pandemic. A total of 25,482 participants, aged 15–79 years, were assessed using an internet survey; the University of California, Los Angeles Loneliness Scale (Version 3), Short Form 3-item (UCLA-LS3-SF3) was used to assess loneliness, and a modified item of the UCLA-LS3-SF3 was used to measure the perception of increased social isolation during the pandemic. The outcome measures included the prevalence/incidence of pain (i.e., headache, neck or shoulder pain, upper limb pain, low back pain, and leg pain), pain intensity, and chronic pain history/prevalence. Pain intensity was measured by the pain/discomfort item of the 5-level version of the EuroQol 5 Dimension scale. Odds ratios of pain prevalence/incidence and chronic pain history/prevalence according to the UCLA-LS3-SF3 scoring groups (tertiles) and the frequency of the perceived increase in social isolation (categories 1–5) were calculated using multinomial logistic regression analysis. The mean pain intensity values among different loneliness and social isolation levels were tested using an analysis of covariance. Increased loneliness and the severity of the perceived social isolation were positively associated with pain prevalence/incidence, intensity, and the history/prevalence of chronic pain.

Introduction

Increased loneliness and social isolation due to the implementation of physical distancing measures and travel restrictions to prevent transmission during the coronavirus disease 2019 (COVID-19) pandemic have adversely affected physical and mental health throughout the world^{1–3}. Loneliness and social isolation are great determinants of health and are associated with quality of life⁴ measures and psychological disorders, such as depression⁵, as well as with physical diseases such as cardiovascular diseases⁶ and increased blood pressure⁷. Moreover, a systematic review reported that loneliness and social isolation were risk factors of early mortality, with an increased likelihood of death ranging from 26–29%⁸.

Loneliness and social isolation are also well-known psychosocial risk factors for the exacerbation of pain^{9,10}. For example, a previous epidemiological study using data from the English Longitudinal Study of Ageing (ELSA) cohort reported that loneliness was associated with the prevalence of musculoskeletal pain¹¹. Therefore, a worsening of psychological stress due to the increased loneliness and social isolation experienced during the COVID-19 pandemic may contribute to the onset of pain¹². Moreover, increased loneliness and social isolation during the COVID-19 pandemic may have a large impact on individuals with chronic pain who have a low tolerance for psychological stress^{12–14}. However, there is lack of direct evidence of an association between pain and increased loneliness and social isolation following the COVID-19 outbreak; this highlights the need for a large population-based study to address an important and urgent health issue.

Loneliness is considered to be felt sad and alone, and no consensus definition currently exists. Based on a review of the literature, Peplau & Perlman (1982) offered the following definition: “the aversive state experienced when a discrepancy exists between the interpersonal relationships one wishes to have, and those that one perceives they currently have;” thus, it is an emotionally unpleasant experience^{15,16}. In addition, two distinct types of loneliness exist, including *emotional loneliness* and *social loneliness*¹⁵. *Emotional loneliness* is defined as “results from the lack of a close, intimate attachment to another person” and *social loneliness* is defined as “results from the lack of a network of social relationships in which the person is part of a group of friends who share common interests and activities”¹⁵. On the other hand, social isolation is structural and can be described objectively based on the characteristics of the situation¹⁷; it is often distinguished from loneliness in an academic context, although loneliness and social isolation are sometimes used collectively, as the concept of social isolation partially overlaps with the concept of *social loneliness*¹⁵.

Therefore, the aims of the present study were to investigate the associations between the loneliness and increased social isolation experienced during the COVID-19 pandemic and (1) the prevalence/incidence of pain (i.e., headache, neck or shoulder pain, upper arm pain, low back pain, and leg pain), (2) pain intensity, and (3) the history/prevalence of chronic pain (pain lasting ≥ 3 months) using data from a large cross-sectional survey of social and health variables related to COVID-19 in Japan.

Methods

Study design

The Japan COVID-19 and Society Internet Survey (JACSIS) was designed to investigate the social and health situation related to the COVID-19 pandemic using an epidemiological approach. In 2020, a total of 28,000 respondents, aged 15–79 years, were selected from 224,389 candidates who received an e-mail invitation among the approximately 2.2 million panelists registered with a Japanese internet survey agency (Rakuten Insight, Inc., Tokyo, Japan <https://in.m.airsurveys.com>). A random sampling method was used to recruit participants using a computer algorithm; the sample was representative of the official Japanese demographic composition as of October 1, 2019 based on categories of age, sex, and living area (i.e., prefecture).

All participants provided web-based informed consent before responding to the online self-report questionnaire.

More specific information pertaining to the JACSIS, along with a detailed description of the method used to recruit participants is described in the Supplementary Methods. The present study employed a cross-sectional design intended to detect changes in biopsychosocial and socioeconomic factors before and after the COVID-19 outbreak.

Study Population

Of 28,000 participants in the JACSIS, we analyzed data from 25,482 participants (12,809 women and 12,673 men) after excluding 2,518 participants who provided invalid responses or met other exclusion criteria; these measures to consistently validate the data quality were performed as described in previous studies^{18,19}. The participants with invalid responses were detected through the use of a dummy item, which stated, “Please choose the option second from

the bottom.” Participants who selected any option other than the one indicated were excluded (n = 1,955). Participants using all recreational substances and medications (i.e., sleeping pills, anxiolytic agents, legal/illegal opioids, cannabis, cocaine, etc.) were excluded, as were those with all chronic diseases (i.e., diabetes, asthma, stroke, ischemic heart disease, cancer, mental disease, etc.); this resulted in the exclusion of 422 and 141 participants, respectively. The characteristics of the 25,482 participants who were included in the final analysis are shown in Supplementary Table 1.

Main Outcome Measures

Loneliness during the COVID-19 pandemic

A Japanese version of the University of California, Los Angeles Loneliness Scale (Version 3), Short Form 3-item (UCLA-LS3-SF3) was used to assess loneliness; the scale was originally developed in English, although both the English and Japanese versions have previously been determined to be valid and reliable^{20,21}. The items were as follows: 1) “How often do you feel that you lack companionship?”; 2) “How often do you feel left out?”; and 3) “How often do you feel isolated from others?” Participants were asked to rate the frequency in which these feelings were experienced over the past 30 days using a five-point scale, ranging from 1 to 5 [1 (Never), 2 (Rarely), 3 (Sometimes), 4 (Often), 5 (Always)]; this was modified from the original UCLA-LS3-SF3, which used a four-point frequency scale. The total UCLA-LS3-SF3 scores in the current study ranged from 3 to 15, with higher scores indicating more severe loneliness. We defined those in the first tertile (3 points), the second tertile (4–5 points), and the third tertile (6–15 points) of the UCLA-LS3-SF3 scores as having ‘no loneliness’, ‘mild loneliness’, and ‘moderate-to-severe loneliness’, respectively. The Cronbach’s alpha value of the internal consistency for the three items was 0.93.

Perception of increased social isolation during the COVID-19 pandemic

The following single question was utilized to measure the perception of increased social isolation during the COVID-19 pandemic: “How often do you feel increased isolation from others compared with how you felt before the COVID-19 outbreak (prior to January 2020)?” The ratings were based on the same five-point frequency scale as the UCLA-LS3-SF3, with responses scored as follows: never (1), rarely (2), sometimes (3), often (4), or always (5). This question was an adaptation of the third item of the UCLA-LS3-SF3; it was modified for the JACSIS to better capture changes in the perceived social isolation between the pre- and post-COVID-19 outbreak timepoints.

Pain

Prevalence And Incidence Of Pain

Participants were asked if they had a headache, neck or shoulder pain, upper limb pain, low back pain, or leg pain; for each type of pain, the responses were categorized as follows: “none”, “yes, it developed before the COVID-19 outbreak”, or “yes, it developed during the COVID-19 pandemic.” Based on these responses, the participants were classified based on one of the following three categories: without pain, the presence of pain since before the COVID-19 outbreak, and pain beginning during the COVID-19 pandemic.

Pain Intensity

Table 3 indicates the differences in reported pain intensity according to the UCLA-LS3-SF3 scoring groups and the frequency with which participants reported an increase in feelings of social isolation. Compared to participants who did not experience loneliness or increased social isolation, those who did reported more severe pain intensity. In Model 2, for individuals who reported any pain symptoms, the adjusted mean pain intensity values among those reporting a lack of loneliness, mild loneliness, and moderate-to-severe loneliness were 1.5, 1.6, and 1.8, respectively; among those reporting increased feelings of social isolation during the COVID-19 pandemic, the adjusted mean pain intensity values for the five frequencies were 1.6, 1.7, 1.8, 1.9, and 2.0.

Table 3
The association of loneliness and a feeling of increased social isolation with pain intensity

| Degree of loneliness | | | | | | | | | | | |
|---|-----|---------------------------------|--------|--|--------|--------------------|---------|-------------------|--------|-------------|---------|
| None 3 points n = 14,277 | | Mild 4–5 points n = 3,250 | | Moderate-to-severe 6–15 points n = 7,955 | | P for trend | | | | | |
| Adjusted mean | SE | Adjusted mean | SE | Adjusted mean | SE | | | | | | |
| Pain intensity for total participants, n = 25,482 | | | | | | | | | | | |
| Model 1 | 1.3 | 0.01 | 1.5*** | 0.01 | 1.7*** | 0.01 | < 0.001 | | | | |
| Model 2 | 1.3 | 0.01 | 1.5*** | 0.01 | 1.6*** | 0.01 | < 0.001 | | | | |
| Pain intensity for individuals with any pain symptoms, n = 15,541 | | | | | | | | | | | |
| Model 1 | 1.5 | 0.01 | 1.6*** | 0.02 | 1.8*** | 0.01 | < 0.001 | | | | |
| Model 2 | 1.5 | 0.01 | 1.6*** | 0.01 | 1.8*** | 0.01 | < 0.001 | | | | |
| Frequency of feelings of increased social isolation during the COVID-19 pandemic | | | | | | | | | | | |
| Never n = 18,168 | | Rarely n = 3,188 | | Sometimes n = 2,454 | | Often n = 1,033 | | Always n = 639 | | P for trend | |
| Adjusted mean | SE | Adjusted mean | SE | Adjusted mean | SE | Adjusted mean | SE | Adjusted mean | SE | | |
| Pain intensity total participants, n = 25,482 | | | | | | | | | | | |
| Model 1 | 1.4 | 0.01 | 1.5*** | 0.01 | 1.6*** | 0.01 | 1.8*** | 0.02 | 2.0*** | 0.03 | < 0.001 |
| Model 2 | 1.4 | 0.01 | 1.5*** | 0.01 | 1.6*** | 0.01 | 1.7*** | 0.02 | 1.8*** | 0.03 | < 0.001 |
| Pain intensity for individuals with any pain symptoms, n = 15,541 | | | | | | | | | | | |
| Model 1 | 1.5 | 0.01 | 1.7*** | 0.02 | 1.8*** | 0.02 | 2.0*** | 0.03 | 2.1*** | 0.03 | < 0.001 |
| Model 2 | 1.6 | 0.01 | 1.7*** | 0.01 | 1.8*** | 0.02 | 1.9*** | 0.03 | 2.0*** | 0.03 | < 0.001 |
| Model 1: Adjusted for age and sex. | | | | | | | | | | | |
| Model 2: Adjusted for age, sex, educational level, marital status, living alone, employment status, equivalized household income, smoking status, alcohol consumption, physical activity, sleep duration, history of depression, and history of mental illnesses other than depression. | | | | | | | | | | | |

History And Prevalence Of Chronic Pain

Table 4 indicates that loneliness and a feeling of increased social isolation were both positively associated with the history and prevalence of chronic pain.

Table 4

The association of loneliness and a feeling of increased social isolation with the history/prevalence of chronic pain during the COVID-19 pandemic

| | Degree of loneliness | | | P for trend | | |
|---|--------------------------------|---------------------------------|--|---------------------------------|---------------------------------|-------------|
| | None 3 points n = 14,277 | Mild 4–5 points n = 3,250 | Moderate-to-Severe 6–15 points n = 7,955 | | | |
| Number with history of chronic pain but already recovered | 734 | 241 | 622 | | | |
| Number with presence of chronic pain | 1,134 | 396 | 1,118 | | | |
| Model 1 | OR (95% CI) | | | | | |
| History of chronic pain but already recovered vs. without history of chronic pain | 1 | 1.60 (1.37–1.86) ^{***} | 2.02 (1.80–2.27) ^{***} | < 0.001 | | |
| Presence of chronic pain vs. without history of chronic pain | 1 | 1.71 (1.51–1.93) ^{***} | 2.44 (2.23–2.68) ^{***} | < 0.001 | | |
| Model 2 | OR (95% CI) | | | | | |
| History of chronic pain but already recovered vs. without history of chronic pain | 1 | 1.42 (1.22–1.66) ^{***} | 1.56 (1.38–1.77) ^{***} | < 0.001 | | |
| Presence of chronic pain vs. without history of chronic pain | 1 | 1.54 (1.36–1.74) ^{***} | 1.81 (1.64–2.00) ^{***} | < 0.001 | | |
| Frequency of feeling of increased social isolation during the COVID-19 pandemic | | | | | | |
| | Never n = 18168 | Rarely n = 3188 | Sometimes n = 2454 | Often n = 1033 | Always n = 639 | P for trend |
| Number with history of chronic pain but already recovered | 1,007 | 265 | 170 | 103 | 52 | |
| Number with presence of chronic pain | 1,707 | 392 | 282 | 163 | 104 | |
| Model 1 | OR (95% CI) | | | OR (95% CI) | OR (95% CI) | |
| History of chronic pain but already recovered vs. without history of chronic pain | 1 | 1.69 (1.47–1.95) ^{***} | 1.54 (1.30–1.83) ^{***} | 2.65 (2.12–3.30) ^{***} | 2.14 (1.59–2.88) ^{***} | < 0.001 |
| Presence of chronic pain vs. without history of chronic pain | 1 | 1.48 (1.32–1.67) ^{***} | 1.55 (1.35–1.78) ^{***} | 2.47 (2.07–2.94) ^{***} | 2.63 (2.11–3.29) ^{***} | < 0.001 |
| Model 2 | OR (95% CI) | | | OR (95% CI) | OR (95% CI) | |
| History of chronic pain but already recovered vs. without history of chronic pain | 1 | 1.44 (1.25–1.67) ^{***} | 1.32 (1.11–1.58) ^{**} | 1.91 (1.51–2.41) ^{***} | 1.48 (1.09–2.02) ^{**} | < 0.001 |
| Presence of chronic pain vs. without history of chronic pain | 1 | 1.26 (1.12–1.43) ^{**} | 1.28 (1.11–1.48) [*] | 1.73 (1.42–2.10) ^{***} | 1.55 (1.21–1.97) [*] | < 0.001 |
| Model 1: Adjusted for age and sex. | | | | | | |
| Model 2: Adjusted for age, sex, educational level, marital status, living alone, employment status, equivalized household income, smoking status, alcohol consumption, physical activity, sleep duration, history of depression, and history of mental illnesses other than depression. | | | | | | |

Potential Confounders

Potential confounders were mainly adapted from previous population-based cohort studies that have examined the associations between psychosocial factors and pain experience [35–37]. These included demographic factors, socioeconomic factors, lifestyle factors, and a history of diseases related to the explanatory and outcome variables.

Demographic factors

We collected data on age (15–19, 20–29, 30–39, 40–49, 50–59, 60–69, or 70–79 years), sex (women or men), and body mass index (quintiles).

Socioeconomic factors

We collected data on the level of education completed (less than high school, high school, vocational school, junior or technical college, university, graduate school, or other), marital status (married or common-law, single, divorced, or widowed), whether the individual was living alone (yes or no), employment status (company executive, owner of a family-operated business, employee of a family-operated business, management-level employee, full-time employee, contract

employee, part-time employee/on-the-side worker, student, retired, full-time homemaker, or unemployed), and equivalized household income (categorized into quintiles).

Equivalized household income was calculated by dividing the median value of the multiple-choice annual household income before-tax by the square root of the number of people living in the household. We defined poverty as an annual equivalized household income of less than 1.22 million JPY, which was the poverty line in 2018 as defined by the Organisation for Economic Co-operation and Development ²².

Life style

We collected data on smoking status (non-smoker, ex-smoker, or current smoker), alcohol consumption (never, ex-drinker, social drinker, < 23 g per day, 23–45 g per day, or ≥ 46 g per day), changes in physical activity before and after the COVID-19 outbreak (decreased, no change, or increased), and sleep duration (< 4 hours, 4–5 hours, 6–7 hours, 8–9 hours, ≥ 10 hours, or hard to respond/unsure). We defined any individual with alcohol consumption ≥ 46 g per day as a heavy drinker.

History of mental diseases

We collected data on the history of depression (categorized as none, a history of depression but already recovered, or comorbid depression) and the history of mental illnesses other than depression (categorized as none, a history of mental illness other than depression but already recovered, or comorbid mental illness other than depression).

Statistical analysis

First, we determined the P for trend of the means and proportions of potential confounders according to the severity of loneliness based on the UCLA-LS3-SF3 scoring groups and the frequency in which participants felt increased social isolation during the COVID-19 pandemic using a general linear model.

Second, we examined the association of loneliness and increased social isolation and the prevalence/incidence of pain experienced during the COVID-19 pandemic. The odds ratios (ORs) of the prevalence and incidence of pain (i.e., headache, neck or shoulder pain, upper limb pain, low back pain, or leg pain) according to the UCLA-LS3-SF-3 scoring groups were calculated using a multinomial logistic regression model, with adjustment for potential confounders.

Third, the overall adjusted mean values of pain intensity for all participants and for individuals with any pain symptoms according to the UCLA-LS3-SF3 scoring groups and the frequency in which feelings of increased social isolation were experienced during the COVID-19 pandemic were tested using an analysis of covariance, with Dunnett's test. Individuals with any pain symptoms were defined as those with headache, neck/shoulder pain, upper limb pain, low back pain, leg pain, or the presence of chronic pain. P values were calculated to compare those reporting a lack of loneliness or those who did not feel an increase in social isolation during the COVID-19 pandemic at all to those of all the other categories.

Finally, we examined the association between the loneliness and increased social isolation felt during the COVID-19 pandemic and the history/prevalence of chronic pain. The ORs of the history and prevalence of chronic pain according to the UCLA-LS3-SF3 scoring groups and the frequency of feelings of increased social isolation were calculated using a multinomial logistic regression model, adjusted for potential confounders.

A multinomial logistic regression analysis is often used to estimate multiple categorical outcomes (i.e., the prevalence/incidence of pain and the history/prevalence of chronic pain).

In addition to the ORs, the P for trends according to the UCLA-LS3-SF3 scoring groups and the frequency of feelings of increased social isolation during the COVID-19 pandemic were calculated using a general linear model.

Model 1 was adjusted for age and sex, whereas Model 2 was adjusted for age, sex, level of education, marital status, living arrangement (living alone or not), employment status, equivalized household income, smoking status, alcohol consumption, physical activity, sleep duration, history of depression, and history of mental illnesses other than depression.

Missing values of potential confounders were used as dummy variables. P values < 0.05 (two-tailed tests) were considered statistically significant. All statistical analyses were performed using Statistical Analysis Software (SAS), Version 9.4 (SAS Institute Inc., Cary, NC, USA).

Ethical Issues

All procedures were conducted in accordance with the ethical standards of the Helsinki Declaration of 1975, as revised in 2013.

The study protocol was reviewed and approved by the Research Ethics Committee of the Osaka International Cancer Institute (approved on June 19, 2020; approval number 20084).

The internet survey agency respected the Act on the Protection of Personal Information in Japan.

All participants provided web-based informed consent before responding to the online questionnaire.

This study was exempted from the obligation to obtain informed consent from the parents/guardians of minors under the age of 18 in Japan. The Ethical Guidelines for Medical and Health Research Involving Human Subjects enforced by Japan's Ministry of Education, Culture, Sports, Science and Technology and Japan's Ministry of Health, Labour and Welfare addressed, "When the research subject has completed junior high school or other relevant schooling, or is 16 years or older, and is considered to have enough judgment concerning the research to be implemented on him/herself, as well as the following matters are prescribed in the research protocol and the chief executive of the research implementing entity approves to carry out the research after relevant ethical review committee deliberation, informed consent shall be obtained not from representative but from the said research subject. (i) The research to be implemented does not involve any invasiveness; and (ii) Information concerning implementation of the research, including purpose of the research and how specimens or information will be handled, is made public, and opportunities to refuse that the research is commenced or continued on the research subject are ensured for

persons who exercise parental authority over the said research subject and guardians of the minor²³." All participants completed junior high school, the present study did not involve any invasiveness, and obtained the approval of the Research Ethics Committee of the Osaka International Cancer Institute. A credit point known as "Epoints", which could be used for internet shopping and cash conversion, was provided to the participants as an incentive.

Results

Descriptive statistics

Of a total of 25,482 participants, 1,033 (4.1%) and 639 (2.5%) participants reported feeling increased social isolation during the COVID-19 pandemic often or always, respectively. The prevalences of headache, neck or shoulder pain, upper limb pain, low back pain, and leg pain were 23.5%, 42.4%, 16.6%, 33.3%, and 17.8%, respectively. The incidences of headache, neck or shoulder pain, upper limb pain, low back pain, and leg pain after the start of the COVID-19 outbreak were 2.0%, 2.4%, 1.8%, 2.1%, 1.5%, respectively. In terms of pain intensity, a total of 7% reported experiencing moderate-to-extreme pain. A total of 6.3% of participants had a history of chronic pain but had already recovered, 3.9% had chronic pain but were receiving treatment, and 6.5% had chronic pain that was not being treated.

The mean values and proportions related to the characteristics of the participants according to their UCLA-LS3-SF3 scoring group and the frequency of feelings of increased social isolation are indicated in Table 1. Compared with participants who did not report experiencing loneliness (the first quartile of the UCLA-LS3-SF3 score), those within the second to fourth quartiles based on the UCLA-LS3-SF3 scores were more likely to be younger and female, to have a lower educational level, to be divorced, to live alone, to be experiencing poverty, to be current smokers, to have decreased their level of physical activity during the COVID-19 pandemic, to sleep less than six hours per night, to have comorbid depression, and to have comorbid mental illnesses other than depression; they were less likely to be obese and heavy drinkers. The prevalence of unemployment did not vary among the UCLA-LS3-SF3 scoring groups.

Table 1
Mean values and proportions for participant characteristics (n = 25,482)

| | Total | | Degree of loneliness | | | | | | Frequency of feelings of increased social isolation during the COVID-19 pandemic | | | | | | | | |
|--|------------|------|----------------------|------|--------------------|------|-----------------------------------|------|--|------------|-------|-----------|--------|-----------|-----------|-----------|-------|
| | | | None 3 points | | Mild 4–5 points | | Moderate-to-severe 6–15 points | | P for trend | | Never | | Rarely | | Sometimes | | Often |
| | n = 25,482 | | n = 14,277 | | n = 3,250 | | n = 7,955 | | | n = 18,168 | | n = 3,188 | | n = 2,454 | | n = 1,033 | |
| | Mean | SD | Mean | SD | Mean | SD | Mean | SD | | Mean | SD | Mean | SD | Mean | SD | Mean | SD |
| Age, years | 48.8 | 17.3 | 51.5 | 17.3 | 50.3 | 17 | 43.3 | 16.2 | < 0.001 | 50.7 | 17.1 | 48.1 | 17.3 | 42.2 | 16.3 | 38.5 | 15 |
| | n | (%) | n | (%) | n | (%) | n | (%) | | n | (%) | n | (%) | n | (%) | n | (%) |
| Women | 12,809 | 50.3 | 6,794 | 47.6 | 1828 | 56.2 | 4187 | 52.6 | < 0.001 | 8809 | 48.5 | 1778 | 55.8 | 1312 | 53.5 | 555 | 53 |
| Body mass index ≥ 25 kg/m ² | 4,910 | 19.3 | 2,864 | 20.1 | 543 | 16.7 | 1,503 | 18.9 | < 0.001 | 3611 | 19.9 | 566 | 17.8 | 431 | 17.6 | 173 | 16 |
| Less than high school graduate | 1,014 | 4.0 | 540 | 3.8 | 93 | 2.9 | 381 | 4.8 | < 0.001 | 718 | 4.0 | 93 | 2.9 | 116 | 4.7 | 45 | 4.4 |
| Divorced | 1,602 | 6.3 | 841 | 5.9 | 212 | 6.5 | 549 | 6.9 | 0.01 | 1107 | 6.1 | 206 | 6.5 | 179 | 7.3 | 60 | 5.8 |
| Living alone | 4,997 | 19.6 | 2,431 | 17.0 | 644 | 19.8 | 1,922 | 24.2 | < 0.001 | 3260 | 17.9 | 688 | 21.6 | 599 | 24.4 | 283 | 27 |
| Unemployed | 3,015 | 11.8 | 1,708 | 12.0 | 374 | 11.5 | 933 | 11.7 | 0.72 | 2266 | 12.5 | 346 | 10.9 | 219 | 8.9 | 85 | 8.2 |
| Living in poverty | 1,393 | 5.5 | 649 | 4.5 | 156 | 4.8 | 588 | 7.4 | < 0.001 | 888 | 4.9 | 178 | 5.6 | 174 | 7.1 | 80 | 7.7 |
| Current smoker | 4,581 | 18.0 | 2,546 | 17.8 | 530 | 16.3 | 1,505 | 18.9 | 0.004 | 3239 | 17.8 | 570 | 17.9 | 447 | 18.2 | 215 | 20 |
| Heavy drinker | 2,144 | 8.4 | 1,284 | 9.0 | 263 | 8.1 | 597 | 7.5 | < 0.001 | 1620 | 8.9 | 238 | 7.5 | 164 | 6.7 | 72 | 7.0 |
| Decreased physical activity during COVID-19 pandemic | 7,358 | 28.9 | 3,774 | 26.4 | 1,022 | 31.4 | 2,562 | 32.2 | < 0.001 | 4712 | 25.9 | 1180 | 37.0 | 766 | 31.2 | 429 | 41 |
| Sleep duration < 6 hours per night | 6,639 | 26.1 | 3,312 | 23.2 | 716 | 22.0 | 2,611 | 32.8 | < 0.001 | 4223 | 23.2 | 862 | 27.0 | 927 | 37.8 | 381 | 36 |
| Comorbid depression | 969 | 3.8 | 172 | 1.2 | 66 | 2.0 | 731 | 9.2 | < 0.001 | 378 | 2.1 | 157 | 4.9 | 181 | 7.4 | 147 | 14 |
| Comorbid mental illnesses other than depression | 950 | 3.7 | 182 | 1.3 | 58 | 1.8 | 710 | 8.9 | < 0.001 | 371 | 2.0 | 158 | 5.0 | 173 | 7.0 | 130 | 12 |

Compared to participants who did not report feeling an increase in social isolation, those who felt more socially isolated during the COVID-19 pandemic were more likely to be younger and obese, to have a lower educational level, to live alone, to be unemployed and living in poverty, to have decreased their level of physical activity during the COVID-19 pandemic, to sleep less than six hours per night, to have comorbid depression, and to have comorbid mental illnesses other than depression; they were also less likely to be heavy drinkers. The prevalences of those who were divorced and those who currently smoked did not vary based on the perceived increase in social isolation.

Prevalence/ Incidence Of Pain

Table 2 indicates that both loneliness and the perception of increased social isolation during the pandemic were positively associated with the prevalence and incidence of all types of pain (i.e., headache, neck or shoulder pain, upper limb pain, low back pain, and leg pain).

Table 2

The association of loneliness and a feeling of increased social isolation with the prevalence/incidence of pain during the COVID-19 pandemic

| | Degree of loneliness | | | P for trend |
|--|----------------------------------|-----------------------------------|--|-------------|
| | None (3 points) n = 14,277 | Mild (4–5 points) n = 3,250 | Moderate-to-Severe (6–15 points) n = 7,955 | |
| Headache | | | | |
| Number with headache since before the COVID-19 outbreak | 2,251 | 888 | 2,848 | |
| Number with headache developed during the COVID-19 pandemic | 150 | 54 | 306 | |
| Model 1 | | OR (95% CI) | OR (95% CI) | |
| Headache since before the COVID-19 outbreak vs. without headache | 1 | 1.92 (1.75–2.11) ^{***} | 2.65 (2.47–2.83) ^{***} | < 0.001 |
| Headache developed during the COVID-19 pandemic vs. without headache | 1 | 1.82 (1.33–2.49) ^{***} | 4.10 (3.31–5.01) ^{***} | < 0.001 |
| Model 2 | | | | |
| Headache since before the COVID-19 outbreak vs. without headache | 1 | 1.78 (1.62–1.95) ^{***} | 2.32 (2.16–2.49) ^{***} | < 0.001 |
| Headache developed during the COVID-19 pandemic vs. without headache | 1 | 1.69 (1.23–2.33) ^{**} | 3.13 (2.53–3.88) ^{***} | < 0.001 |
| Neck or shoulder pain | | | | |
| Number with neck or shoulder pain since before the COVID-19 outbreak | 4972 | 1665 | 4166 | |
| Number with neck or shoulder pain developed during the COVID-19 pandemic | 204 | 65 | 333 | |
| Model 1 | | OR (95% CI) | OR (95% CI) | |
| Neck or shoulder pain since before the COVID-19 outbreak vs. without neck or shoulder pain | 1 | 1.94 (1.79–2.10) ^{***} | 2.21 (2.09–2.35) ^{***} | < 0.001 |
| Neck or shoulder pain developed during the COVID-19 pandemic vs. without neck or shoulder pain | 1 | 1.86 (1.40–2.47) ^{***} | 3.84 (3.20–4.60) ^{***} | < 0.001 |
| Model 2 | | | | |
| Neck or shoulder pain since before the COVID-19 outbreak vs. without neck or shoulder pain | 1 | 1.78 (1.64–1.93) ^{***} | 2.05 (1.93–2.19) ^{***} | < 0.001 |
| Neck or shoulder pain developed during the COVID-19 pandemic vs. without neck or shoulder pain | 1 | 1.69 (1.27–2.25) ^{***} | 3.02 (2.48–3.66) ^{***} | < 0.001 |
| Upper limb pain | | | | |
| Number with upper limb pain since before the COVID-19 outbreak | 1736 | 596 | 1904 | |
| Number with upper limb pain developed during the COVID-19 pandemic | 161 | 49 | 253 | |
| Model 1 | | OR (95% CI) | OR (95% CI) | |
| Upper limb pain since before the COVID-19 outbreak vs. without upper limb pain | 1 | 1.64 (1.48–1.82) ^{***} | 2.71 (2.52–2.93) ^{***} | < 0.001 |
| Upper limb pain developed during the COVID-19 pandemic vs. without upper limb pain | 1 | 1.42 (1.03–1.96) [*] | 3.28 (2.67–4.03) ^{***} | < 0.001 |
| Model 2 | | | | |
| Upper limb pain since before the COVID-19 outbreak vs. without upper limb pain | 1 | 1.53 (1.38–1.70) ^{***} | 2.30 (2.13–2.50) ^{***} | < 0.001 |
| Upper limb pain developed during the COVID-19 pandemic vs. without upper limb pain | 1 | 1.32 (0.95–1.83) | 2.57 (2.06–3.19) ^{***} | < 0.001 |

Model 1: Adjusted for age and sex.

Model 2: Adjusted for age, sex, educational level, marital status, living alone, employment status, equivalized household income, smoking status, alcohol consumption, physical activity, sleep duration, history of depression, and history of mental illnesses other than depression.

| Degree of loneliness | | | | | | |
|---|-------------------|---------------------------------|---------------------------------|---------------------------------|----------------------------------|--------------------|
| Low back pain | | | | | | |
| Number with low back pain since before the COVID-19 outbreak | 3942 | 1298 | 3247 | | | |
| Number with low back pain developed during the COVID-19 pandemic | 194 | 65 | 275 | | | |
| Model 1 | | OR (95% CI) | OR (95% CI) | | | |
| Low back pain since before the COVID-19 outbreak vs. without low back pain | 1 | 1.79 (1.65–1.94) ^{***} | 2.11 (1.99–2.24) ^{***} | < 0.001 | | |
| Low back pain developed during the COVID-19 pandemic vs. without low back pain | 1 | 1.78 (1.36–2.41) ^{***} | 3.14 (2.59–3.81) ^{***} | < 0.001 | | |
| Model 2 | | | | | | |
| Low back pain since before the COVID-19 outbreak vs. without low back pain | 1 | 1.66 (1.53–1.80) ^{***} | 1.95 (1.83–2.08) ^{***} | < 0.001 | | |
| Low back pain developed during the COVID-19 pandemic vs. without low back pain | 1 | 1.67 (1.25–2.23) ^{***} | 2.40 (1.95–2.95) ^{***} | < 0.001 | | |
| Leg pain | | | | | | |
| Number with leg pain since before the COVID-19 outbreak | 2030 | 666 | 1828 | | | |
| Number with leg pain developed during the COVID-19 pandemic | 136 | 46 | 195 | | | |
| Model 1 | | OR (95% CI) | OR (95% CI) | | | |
| Leg pain since before the COVID-19 outbreak vs. without leg pain | 1 | 1.61 (1.45–1.77) ^{***} | 2.37 (2.20–2.55) ^{***} | < 0.001 | | |
| Leg pain developed during the COVID-19 pandemic vs. without leg pain | 1 | 1.60 (1.14–2.24) ^{**} | 3.23 (2.57–4.06) ^{***} | < 0.001 | | |
| Model 2 | | | | | | |
| Leg pain since before the COVID-19 outbreak vs. without leg pain | 1 | 1.52 (1.37–1.68) ^{***} | 2.05 (1.89–2.22) ^{***} | < 0.001 | | |
| Leg pain developed during the COVID-19 pandemic vs. without leg pain | 1 | 1.54 (1.09–2.16) [*] | 2.45 (1.92–3.13) ^{***} | < 0.001 | | |
| Frequency of feelings of increased social isolation during the COVID-19 pandemic | | | | | | |
| | Never | Rarely | Sometimes | Often | Always | P for trend |
| | n = 1,8168 | n = 3,188 | n = 2,454 | n = 1,033 | n = 639 | |
| Headache | | | | | | |
| Number with headache since before the COVID-19 outbreak | 3,586 | 966 | 768 | 398 | 269 | |
| Number with headache developed during the COVID-19 pandemic | 231 | 63 | 88 | 74 | 54 | |
| Model 1 | | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | |
| Headache since before the COVID-19 outbreak vs. without headache | 1 | 1.65 (1.51–1.80) ^{***} | 1.55 (1.41–1.71) ^{***} | 2.15 (1.87–2.47) ^{***} | 2.55 (2.15–3.03) ^{***} | < 0.001 |
| Headache developed during the COVID-19 pandemic vs. without headache | 1 | 1.69 (1.27–2.24) ^{***} | 2.70 (2.09–3.48) ^{***} | 5.93 (4.48–7.85) ^{***} | 7.66 (5.56–10.57) ^{***} | < 0.001 |
| Model 2 | | | | | | |
| Headache since before the COVID-19 outbreak vs. without headache | 1 | 1.53 (1.40–1.68) ^{***} | 1.48 (1.34–1.64) ^{***} | 1.84 (1.58–2.13) ^{***} | 2.08 (1.73–2.49) ^{***} | < 0.001 |
| Headache developed during the COVID-19 outbreak vs. without headache | 1 | 1.41 (1.06–1.88) [*] | 2.16 (1.66–2.81) ^{***} | 4.04 (3.00–5.45) ^{***} | 5.21 (3.71–7.33) ^{***} | < 0.001 |
| Neck or shoulder pain | | | | | | |
| Number with neck or shoulder pain since before the COVID-19 outbreak | 7162 | 1596 | 1152 | 554 | 339 | |
| Model 1: Adjusted for age and sex. | | | | | | |
| Model 2: Adjusted for age, sex, educational level, marital status, living alone, employment status, equivalized household income, smoking status, alcohol consumption, physical activity, sleep duration, history of depression, and history of mental illnesses other than depression. | | | | | | |

| Degree of loneliness | | | | | | |
|---|------|---------------------|---------------------|---------------------|-----------------------|---------|
| Number with neck or shoulder pain developed during the COVID-19 pandemic | 282 | 88 | 91 | 79 | 62 | |
| Model 1 | | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | |
| Neck or shoulder pain since before the COVID-19 outbreak vs. without neck or shoulder pain | 1 | 1.54 (1.42–1.66)*** | 1.37 (1.26–1.49)*** | 2.05 (1.79–2.35)*** | 2.09 (1.76–2.48)*** | < 0.001 |
| Neck or shoulder pain developed during the COVID-19 pandemic vs. without neck or shoulder pain | 1 | 2.13 (1.66–2.72)*** | 2.56 (2.00–3.27)*** | 6.46 (4.91–8.50)*** | 8.47 (6.22–11.53)*** | < 0.001 |
| Model 2 | | | | | | |
| Neck or shoulder pain since before the COVID-19 outbreak vs. without neck or shoulder pain | 1 | 1.45 (1.34–1.57)*** | 1.42 (1.30–1.56)*** | 1.88 (1.63–2.17)*** | 1.84 (1.53–2.21)*** | < 0.001 |
| Neck or shoulder pain developed during the COVID-19 pandemic vs. without neck or shoulder pain | 1 | 1.77 (1.38–2.27)*** | 2.11 (1.63–2.73)*** | 4.52 (3.37–6.04)*** | 5.97 (4.31–8.27)*** | < 0.001 |
| Upper limb pain | | | | | | |
| Number with upper limb pain since before the COVID-19 outbreak | 2609 | 667 | 510 | 266 | 184 | |
| Number with upper limb pain developed during the COVID-19 pandemic | 215 | 66 | 80 | 62 | 40 | |
| Model 1 | | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | |
| Upper limb pain since before the COVID-19 outbreak vs. without upper limb pain | 1 | 1.64 (1.49–1.80)*** | 1.82 (1.64–2.03)*** | 2.69 (2.31–3.13)*** | 3.18 (2.65–3.81)*** | < 0.001 |
| Upper limb pain developed during the COVID-19 pandemic vs. without upper limb pain | 1 | 1.90 (1.44–2.51)*** | 3.05 (2.34–3.98)*** | 6.27 (4.65–8.47)*** | 6.86 (4.79–9.82)*** | < 0.001 |
| Model 2 | | | | | | |
| Upper limb pain since before the COVID-19 outbreak vs. without upper limb pain | 1 | 1.51 (1.37–1.67)*** | 1.68 (1.50–1.88)*** | 2.20 (1.87–2.57)*** | 2.44 (2.01–2.96)*** | < 0.001 |
| Upper limb pain developed during the COVID-19 pandemic vs. without upper limb pain | 1 | 1.61 (1.21–2.14)** | 2.51 (1.91–3.31)*** | 4.31 (3.13–5.93)*** | 4.70 (3.22–6.86)*** | < 0.001 |
| Low back pain | | | | | | |
| Number with low back pain since before the COVID-19 outbreak | 5673 | 1252 | 869 | 426 | 267 | |
| Number with low back pain developed during the COVID-19 pandemic | 257 | 66 | 88 | 69 | 54 | |
| Model 1 | | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | |
| Low back pain since before the COVID-19 outbreak vs. without low back pain | 1 | 1.48 (1.37–1.60)*** | 1.38 (1.26–1.51)*** | 1.97 (1.72–2.25)*** | 2.09 (1.77–2.48)*** | < 0.001 |
| Low back pain developed during the COVID-19 pandemic vs. without low back pain | 1 | 1.69 (1.28–2.22)*** | 2.78 (2.16–3.57)*** | 6.02 (4.52–8.02)*** | 7.98 (5.79–11.00)*** | < 0.001 |
| Model 2 | | | | | | |
| Low back pain since before the COVID-19 outbreak vs. without low back pain | 1 | 1.41 (1.30–1.53)*** | 1.39 (1.27–1.53)*** | 1.85 (1.61–2.13)*** | 1.85 (1.55–2.21)*** | < 0.001 |
| Low back pain developed during the COVID-19 pandemic vs. without low back pain | 1 | 1.42 (1.08–1.88)* | 2.30 (1.77–2.99)*** | 4.11 (3.03–5.59)*** | 5.48 (3.90–7.70)*** | < 0.001 |
| Leg pain | | | | | | |
| Number with leg pain since before the COVID-19 outbreak | 2943 | 705 | 460 | 237 | 179 | |
| Number with leg pain developed during the COVID-19 pandemic | 178 | 49 | 57 | 52 | 41 | |
| Model 1 | | OR (95% CI) | OR (95% CI) | OR (95% CI) | OR (95% CI) | |
| Leg pain since before the COVID-19 outbreak vs. without leg pain | 1 | 1.57 (1.43–1.73)*** | 1.52 (1.36–1.70)*** | 2.29 (1.96–2.68)*** | 3.14 (2.60–3.77)*** | < 0.001 |
| Leg pain developed during the COVID-19 pandemic vs. without leg pain | 1 | 1.75 (1.27–2.40)*** | 2.83 (2.08–3.85)*** | 7.19 (5.17–9.99)*** | 10.14 (7.04–14.61)*** | < 0.001 |
| Model 2 | | | | | | |
| Model 1: Adjusted for age and sex. | | | | | | |
| Model 2: Adjusted for age, sex, educational level, marital status, living alone, employment status, equivalized household income, smoking status, alcohol consumption, physical activity, sleep duration, history of depression, and history of mental illnesses other than depression. | | | | | | |

| | | Degree of loneliness | | | | | |
|---|---|---------------------------------|---------------------------------|---------------------------------|----------------------------------|---------|--|
| Leg pain since before the COVID-19 outbreak vs. without leg pain | 1 | 1.45 (1.32–1.60) ^{***} | 1.39 (1.24–1.57) ^{***} | 1.86 (1.58–2.20) ^{***} | 2.46 (2.102–2.99) ^{***} | < 0.001 | |
| Leg pain developed during the COVID-19 pandemic vs. without leg pain | 1 | 1.51 (1.09–2.10) ^{***} | 2.20 (1.60–3.03) ^{***} | 4.91 (3.45–6.98) ^{***} | 6.83 (4.63–10.09) ^{***} | < 0.001 | |
| Model 1: Adjusted for age and sex. | | | | | | | |
| Model 2: Adjusted for age, sex, educational level, marital status, living alone, employment status, equalized household income, smoking status, alcohol consumption, physical activity, sleep duration, history of depression, and history of mental illnesses other than depression. | | | | | | | |

Discussion

The predominant location where participants reported experiencing pain during the COVID-19 pandemic was the neck or shoulders, followed by low back pain. Of the total number of participants, 6.3% reported a prior history of chronic pain, and 10.4% were presently experiencing chronic pain. Both loneliness and a perception of increased social isolation during the COVID-19 pandemic were positively associated with the prevalence/incidence of all types of pain, pain intensity, and a history/prevalence of chronic pain in a dose-response manner.

To the best of our knowledge, the present study is the first to provide direct evidence of the impact that loneliness and the perception of increased social isolation during the COVID-19 pandemic has had on individuals with pain. We assumed several underlying mechanisms that could explain these findings.

In general, loneliness and social isolation are factors associated with psychological stress and distress that can induce depressive symptoms^{24,25}, and a previous meta-analysis revealed that loneliness had a moderate impact on depression⁵. Depressive symptoms have been shown to be comorbid with pain and increased pain intensity^{26,27}; in turn, loneliness and social isolation would be associated with increased pain responses or perceptions mediated by depressive symptoms, even in the absence of an actual COVID-19 infection.

As a biophysiological mechanism, social isolation may decrease the threshold of pain sensitivity²⁸. In animal models, social isolation in rodents has been shown to result in reduced pain thresholds^{28,29}; for example, in group-housed mice with immobilization stress, increased pain thresholds have been reported following morphine administration, although this effect was not observed in socially isolated mice²⁸. Thus, social isolation due to the COVID-19 pandemic could increase the perception of pain in humans, as increased pain intensity could be mediated by a reduction in pain thresholds.

A previous cohort study investigated the impact of a catastrophic event on pain responses in humans; the study examined those with pain before and approximately six months after the September 11th terrorist attacks in New York and New Jersey, showing that residents reported an increased prevalence of musculoskeletal pain, but not pain from fibromyalgia, after the terrorist attacks³⁰. Although the impact of a terrorism event on health may differ from that of a pandemic, and although we did not investigate fibromyalgia, the results of the present study are consistent with the reported changes in musculoskeletal pain.

The findings of the present study indicate that it is important for healthcare providers and policymakers to pay attention to the increased loneliness and social isolation experienced during the COVID-19 pandemic because they may be associated with an increased incidence and worsening of pain symptoms, and the changes may be exacerbated in individuals who have a past history of or are currently experiencing chronic pain.

A strength of the present study was that it included a large, population-based sample of approximately 25,000 individuals, providing sufficient statistical power for analysis. The present study had several limitations, however. First, we could not determine whether individual participants had been diagnosed with COVID-19 or not. An actual COVID-19 infection could be a potential cofounder in the present study, as individuals who were COVID-19-positive would have been required to adhere to strict social isolation procedures over a couple of weeks. Second, we examined participants' perceptions of increased social isolation and did not objectively examine the impact of this social isolation on pain (e.g., based on geographical conditions and events). Objective details about social isolation could provide additional useful information. Third, the web-based survey may have biased the distribution and the present study may not be truly representative of the general population, although the demographic profile of the participants was consistent with the official Japanese demographic composition based on the Japanese Vital Statistics for age, sex, and living area as of October 1, 2019³¹. The current prevalence of chronic pain (pain duration \geq 3 months; 10.4%) was one-quarter of that described in a previous report (39.3%) that was based on a postal survey of Japanese adults, aged 20 years or older, living in a single city³². The prevalence of chronic pain reported in previous web-based surveys was approximately 20%, although these studies were limited by the fact that they only assessed those with moderate-to-severe pain intensity (numerical rating scale score of \geq 5 out of 10)^{33,34}. This discrepancy may be a result of the fact that the present study included more healthy individuals compared with previous surveys. In addition, the participants who were recruited in previous surveys may have had a more particular interest in pain compared with the general population; therefore, the current study population may have been more representative than those of previous reports. Finally, there may have been some recall bias in this study, as it used a cross-sectional design; thus, temporal aspects cannot be discussed. For example, individuals experiencing pain who felt increased social isolation following the COVID-19 outbreak may be more likely to recall the onset of their pain as being related to the pandemic. Future studies will need to clarify this using a prospective design.

In conclusion, in accordance with their severity, loneliness and the perception of increased social isolation during the COVID-19 pandemic were positively associated with the prevalence/incidence of pain, pain intensity, and the history/prevalence of chronic pain. These findings suggest that loneliness and social isolation should be considered, especially as they relate to pain experienced during the COVID-19 pandemic period.

Declarations

Acknowledgments

The authors are grateful to all the respondents in this study. The authors also appreciate Dr. Masako Iseki, Department of Anesthesiology and Pain Medicine, Juntendo University Faculty of Medicine, Japan for her professional advises. This study was funded by the Japan Society for the Promotion of Science (JSPS) KAKENHI Grants [grant number 17H03589;19K10671;19K10446;18H03107; 18H03062], the JSPS Grant-in-Aid for Young Scientists [grant number 19K19439], Research Support Program to Apply the Wisdom of the University to tackle COVID-19 Related Emergency Problems, University of Tsukuba, and a Health Labour Sciences Research Grant [grant number 19FA1005;19FG2001]. This research was partially supported by the JSPS Overseas Research Fellowships (to K.Y.). The findings and conclusions of this article are the sole responsibility of the authors and do not represent the official views of the research funders. We would like to thank Editage (www.editage.com) for English language editing. The authors report no conflicts of interest.

Competing Interest: The author(s) declare no competing interests.

Data availability statement: The data used in this study are not available in a public repository because they contain personally identifiable or potentially sensitive patient information. Based on the regulations for ethical guidelines in Japan, the Research Ethics Committee of the Osaka International Cancer Institute has imposed restrictions on the dissemination of the data collected in this study. All data enquiries should be addressed to the person responsible for data management, Dr. Takahiro Tabuchi at the following e-mail address: tabuchitak@gmail.com.

Author contribution statement: Design and conceptualized study, analyzed the data and drafted the manuscript for intellectual content (KY); and interpreted the data, revised the manuscript for intellectual content (KW, YK, HM, and TT).

References

1. Smith, B. J. & Lim, M. H. How the COVID-19 pandemic is focusing attention on loneliness and social isolation. *Public Heal. Res. Pract.* **30**, 2–5 (2020).
2. Banerjee, D. & Rai, M. Social isolation in Covid-19: The impact of loneliness. *Int. J. Soc. Psychiatry* **66**, 525–527 (2020).
3. Killgore, W. D. S., Cloonan, S. A., Taylor, E. C. & Dailey, N. S. Loneliness: A signature mental health concern in the era of COVID-19. *Psychiatry Res.* **290**, 113117 (2020).
4. Liu, L. J. & Guo, Q. Loneliness and health-related quality of life for the empty nest elderly in the rural area of a mountainous county in China. *Qual. Life Res.* **16**, 1275–1280 (2007).
5. Erzen, E. & Çikrikci, Ö. The effect of loneliness on depression: A meta-analysis. *Int. J. Soc. Psychiatry* **64**, 427–435 (2018).
6. Sorkin, D., Rook, K. S. & Lu, J. L. Loneliness, lack of emotional support, lack of companionship, and the likelihood of having a heart condition in an elderly sample. *Ann. Behav. Med.* **24**, 290–8 (2002).
7. Hawkey, L. C., Thisted, R. A., Masi, C. M. & Cacioppo, J. T. Loneliness predicts increased blood pressure: 5-year cross-lagged analyses in middle-aged and older adults. *Psychol. Aging* **25**, 132–41 (2010).
8. Holt-Lunstad, J., Smith, T. B., Baker, M., Harris, T. & Stephenson, D. Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspect. Psychol. Sci.* **10**, 227–37 (2015).
9. Wolf, L. D. & Davis, M. C. Loneliness, daily pain, and perceptions of interpersonal events in adults with fibromyalgia. *Health Psychol.* **33**, 929–37 (2014).
10. Karayannis, N. V., Baumann, I., Sturgeon, J. A., Melloh, M. & Mackey, S. C. The Impact of Social Isolation on Pain Interference: A Longitudinal Study. *Ann. Behav. Med.* **53**, 65–74 (2019).
11. Smith, T. O., Dainty, J. R., Williamson, E. & Martin, K. R. Association between musculoskeletal pain with social isolation and loneliness: analysis of the English Longitudinal Study of Ageing. *Br. J. pain* **13**, 82–90 (2019).
12. Karos, K. *et al.* The social threats of COVID-19 for people with chronic pain. *Pain* **161**, 2229–2235 (2020).
13. Clauw, D. J., Häuser, W., Cohen, S. P. & Fitzcharles, M.-A. Considering the potential for an increase in chronic pain after the COVID-19 pandemic. *Pain* **161**, 1694–1697 (2020).
14. Chaturvedi, S. K. Health anxiety, health-related life events, and somatization during COVID-19 pandemic can increase chronic pain. *Pain* **161**, 2652 (2020).
15. Heinrich, L. M. & Gullone, E. The clinical significance of loneliness: A literature review. *Clin. Psychol. Rev.* **26**, 695–718 (2006).
16. Perlman, D. & Peplau, L. A. Perspectives on loneliness. in *Loneliness: a sourcebook of current theory, research, and therapy* 1–18 (Wiley, 1982).
17. Gierveld, J. D. J. & Tilburg, T. Van. A 6-Item Scale for Overall, Emotional, and Social Loneliness. *Res. Aging* **28**, 582–598 (2006).
18. Tabuchi, T. *et al.* Heat-not-burn tobacco product use in Japan: its prevalence, predictors and perceived symptoms from exposure to secondhand heat-not-burn tobacco aerosol. *Tob. Control* **27**, e25–e33 (2018).
19. Tabuchi, T., Shinozaki, T., Kunugita, N., Nakamura, M. & Tsuji, I. Study Profile: The Japan ‘Society and New Tobacco’ Internet Survey (JASTIS): A Longitudinal Internet Cohort Study of Heat-Not-Burn Tobacco Products, Electronic Cigarettes, and Conventional Tobacco Products in Japan. *J. Epidemiol.* **29**, 444–450 (2019).
20. Arimoto, A. & Tadaka, E. Reliability and validity of Japanese versions of the UCLA loneliness scale version 3 for use among mothers with infants and toddlers: A cross-sectional study. *BMC Womens. Health* **19**, 3–9 (2019).
21. Hughes, M. E., Waite, L. J., Hawkey, L. C. & Cacioppo, J. T. A Short Scale for Measuring Loneliness in Large Surveys: Results From Two Population-Based Studies. *Res. Aging* **26**, 655–672 (2004).

22. The Ministry of Health Labour and Welfare. Comprehensive Survey of Living Conditions in 2019 (in Japanese). (2019). Available at: <https://www.mhlw.go.jp/toukei/saikin/hw/k-tyosa/k-tyosa19/dl/03.pdf>. (Accessed: 2nd November 2020)
23. Japan's Ministry of Education, Culture, Sports Science and Technology and Japan's Ministry of Health, Labour and Welfare. the Ethical Guidelines for Medical and Health Research Involving Human Subjects (Provisional Translation as of March 2015). (2014). Available at: <https://www.mhlw.go.jp/file/06-Seisakujouhou-10600000-Daijinkanboukouseikagakuka/0000080278.pdf>. (Accessed: 9th March 2021)
24. Cacioppo, J. T., Hawkley, L. C. & Thisted, R. A. Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. *Psychol. Aging* **25**, 453–63 (2010).
25. Bodner, E. & Bergman, Y. S. Loneliness and depressive symptoms among older adults: The moderating role of subjective life expectancy. *Psychiatry Res.* **237**, 78–82 (2016).
26. Leino, P. & Magni, G. Depressive and distress symptoms as predictors of low back pain, neck-shoulder pain, and other musculoskeletal morbidity: a 10-year follow-up of metal industry employees. *Pain* **53**, 89–94 (1993).
27. Bair, M. J., Robinson, R. L., Katon, W. & Kroenke, K. Depression and pain comorbidity: a literature review. *Arch. Intern. Med.* **163**, 2433–2445 (2003).
28. Puglisi-Allegra, S. & Oliverio, A. Social isolation: effects on pain threshold and stress-induced analgesia. *Pharmacol. Biochem. Behav.* **19**, 679–81 (1983).
29. Coudereau, J. P., Monier, C., Bourre, J. M. & Frances, H. Effect of isolation on pain threshold and on different effects of morphine. *Prog. Neuropsychopharmacol. Biol. Psychiatry* **21**, 997–1018 (1997).
30. Raphael, K. G., Natelson, B. H., Janal, M. N. & Nayak, S. A community-based survey of fibromyalgia-like pain complaints following the World Trade Center terrorist attacks. *Pain* **100**, 131–9 (2002).
31. The Ministry of Health Labour and Welfare. Vital Statistics. (2019). Available at: <https://www.e-stat.go.jp/en/stat-search/files?page=1&toukei=00450011&tstat=000001028897>. (Accessed: 12th November 2020)
32. Inoue, S. *et al.* Chronic Pain in the Japanese Community—Prevalence, Characteristics and Impact on Quality of Life. *PLoS One* **10**, e0129262 (2015).
33. Matsudaira, K. *et al.* Pain associated cross-sectional epidemiological (PACE) survey 2009 (in Japanese). *Pain Clin.* **32**, 1345–1356 (2011).
34. Yabuki, S. *et al.* A nationwide survey of chronic pain sufferers in Japan (in Japanese). *Clin. Orthop* **47**, 127–134 (2012).

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- [03SupMaterial20210223.pdf](#)