

Association of living condition using urbanisation level and neighbourhood deprivation with loneliness and social isolation during COVID-19 pandemic: a cross-sectional study of the nationwide data in Japan

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To cite: Sasaki N, Tabuchi T, Okubo R, *et al.* Association of living condition using urbanisation level and neighbourhood deprivation with loneliness and social isolation during COVID-19 pandemic: a cross-sectional study of the nationwide data in Japan. *BMJ Public Health* 2023;1:e000341. doi:10.1136/bmjph-2023-000341

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjph-2023-000341>).

Received 26 June 2023
Accepted 20 October 2023



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ABSTRACTS

Objectives The aim of this study was to investigate the association of living condition (deprivation and urbanisation level) with loneliness and social isolation.

Study design Cross-sectional study.

Methods Data were retrieved from the Japan COVID-19 and Society Internet Survey, a nationwide online cohort study, conducted from September to October 2021. Area Deprivation Index and Densely Inhabited District data were used as indicators of living condition. The Japanese version of the University of California, Los Angeles Loneliness Scale and Lubben Social Network Scale-6 were used to assess loneliness and social isolation, respectively. Analysis of covariance was performed to compare the difference in outcome variables by living conditions (four categories), adjusting for gender, age, educational attainment, income, marital status, people living with, work status and subjective health status.

Results A total of 27 520 community dwelling people were included in this study. For loneliness, living condition did not show a significant difference in the adjusted model, while deprived area had a tendency to show high loneliness. For social isolation, there was a significant group difference in the adjusted model ($p < 0.001$), and living in a higher urbanisation level and lower deprivation showed the highest score for social isolation.

Conclusion Overall, the effects of the living condition on loneliness and social isolation were small. Further study is needed to explore more comprehensive environment factors affecting loneliness and social isolation.

INTRODUCTION

Loneliness and social isolation are important public health concerns that need to be addressed, especially during periods of social change such as a pandemic. Loneliness and social isolation are associated with all-cause mortality,^{1–3} coronary heart disease and stroke,⁴ depression^{5,6} and impaired cognitive function.⁷

WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Loneliness and social isolation are important public health concerns.
- ⇒ Urbanisation and deprivation (U&D) are important social determinants of health.

WHAT THIS STUDY ADDS

- ⇒ This was the first study to examine simultaneously U&D on loneliness and isolation.
- ⇒ Social isolation was more associated with urbanisation.
- ⇒ Loneliness and social isolation were not greatly affected by the two factors.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Simple indicators of U&D may not be enough to grasp loneliness and social isolation.
- ⇒ Future study is needed to investigate the environmental factors affecting loneliness and isolation.

Social isolation is an objective and quantifiable view of social network size and contact. Loneliness is an individual's subjective experience about the lack of satisfying social relationships.⁸ While both outcomes are related to health risk and they are of a similar concept, social isolation and loneliness are often not greatly correlated^{9,10} due to their distinctive definitions. Loneliness is a more subjective emotion, whereas social isolation has more objective lack of relationships and social interaction.⁹ Loneliness is higher in women, with advanced age, low education, unmarried/widow, unemployment, lower income and living alone.^{11–14} Many of the predictors are the same as social isolation in spite of cultural dependent variations, except for gender^{15,16}; possibly explained by cultural masculine normativity.¹⁷ Investigating both

outcomes individually can, thus, provide insights to support effective public health strategies, not only at an individual-level but also for environment-level measurements.

Recently, living condition, including urbanisation and deprivation, has become regarded as important social determinants of health.¹⁸ Contemporary evidence is growing about the relationship between urbanisation and mental health,^{19–25} which a review suggested the negative effect of urbanisation on mental health.²⁰ Regarding loneliness, studies using simple measurement (eg, density) found no associations with loneliness especially when the perceived quality of neighbourhood is controlled.^{25–27} Living in rural area is also not associated with loneliness,^{28,29} or is associated, but with a small effect,³⁰ while rurality moderates social resources.³¹ In comparison, some studies found that urban living is associated with social isolation,^{28,32,33} but there is another study showing no association.^{11,34} As a potential mechanism, urbanisation may increase feelings of loneliness and isolation as individuals attempt to avoid unwanted social interactions, and the potential reduction in social connectivity resulting from rural-to-urban migration, which leads inhibition of a sense of belonging.³⁵ Yet, the association of urbanisation with loneliness and isolation needs further research.^{36–38}

In particular, there are many adverse health consequences in deprived areas, without essential things to life, society and living well. Living in a high deprivation level area is associated with high all-cause mortality,³⁹ a short healthy life expectancy⁴⁰ and poor mental health.^{41–43} One study reported that people living in a high deprived area showed high levels of loneliness, but the significance disappeared after adjusting for individual social relationship.²⁹ The influence of neighbourhood deprivation on social isolation is also controversial; with one study finding small effects,⁴⁴ and another no association.⁴⁵ As a potential mechanism, living in a deprived area adds barriers to social engagement due to low incomes, or disjointed services, fear of crime and high residential turnover.^{43,46} As noted, there were some studies examining the association of urbanisation and deprivation with loneliness and isolation, respectively, but living condition should be examined by considering interactions of both indicators because urbanisation and deprivation can be inter-related and there may be areas where both characteristics are mixed (eg, slum, exclusive residential district). Moreover, understanding levels of loneliness and social isolation specific to each region can be beneficial in tailoring mental health and public health interventions during the pandemic for each respective area. However, there are few studies considering urbanisation and deprivation at the same time to assess loneliness and social isolation during COVID-19 pandemic.

Thus, this study aimed to investigate the association between living condition (deprivation and urbanisation level) and loneliness and social isolation, using data from a nationwide survey during COVID-19 pandemic in Japan.

METHODS

Study design and participants

This study used a sample from the Japan COVID-19 and Society Internet Survey (JACSIS), a nationwide online cohort study to assess sociohealth inequity caused by pandemic.⁴⁷ Details of the study design have been described elsewhere.⁴⁸ This cross-sectional study used the JACSIS data obtained from September to October 2021. Following the Tokyo Olympics in the summer of 2021, Japan experienced a fifth wave of outbreaks. The survey was conducted during the latter stages of this outbreak. Participants were invited from the baseline JACSIS respondents, which was conducted from August to September in 2020, and newly invited research panelists (aged 15–79 years) from a large internet survey company (Rakuten Insight, <https://insight.rakuten.co.jp/>). Potential participants were selected at baseline by each sex, age and prefecture category (covering all 47 prefectures) using a simple random sampling representative of the official Japanese demographic composition as of 1 October 2019, from approximately 2.2 million panelists. A total of 31 000 data were collected. To validate data quality, we excluded respondents showing discrepancies and/or artificial/unnatural responses by using three questions, following a previous study.⁴⁹

Measurements

Living condition

The Area Deprivation Index (ADI) was used as an indicator of neighbourhood deprivation. Data were derived from the 2010 Population Census of Japan. Details of this ADI are described elsewhere.³⁹ This composite indicator comprises weighted sums of poverty-related census variables such as unemployment rate and proportion of elderly couple households, elderly single-occupier households, single mother households, rented houses, sales and service workers, agricultural workers and blue-collar workers. A higher ADI score indicates more neighbourhood deprivation. ADI was dichotomised into high and low.

Although there are several ways to assess urbanisation (eg, population density, number of people there, quality of being urbanised), Densely Inhabited District (DID) data were used as an indicator of urbanisation level in this study. The data were derived from the 2015 Population Census of Japan (https://nlftp.mlit.go.jp/ksj/gml/datalist/KsjTmplt-A16-v2_3.html). A higher DID score indicates a greater urbanisation level. DID was dichotomised into high and low.

Both ADI and DID were created at a zip code level in Japan (113 107 zip codes, each with approximately 1100 people living within each zip code).

Loneliness

A Japanese version of the University of California, Los Angeles Loneliness Scale (V.3), Short Form 3-item (UCLA-LS3-SF3) was used to assess loneliness with four response options: (1) never (score=1), (2) rarely (=1), (3) sometimes (=2), (4) always (=3). The total score is

the sum of all items, which ranges from 3 to 9. The three items asked the frequency of 'feel that they lack companionship', 'feel left out' and 'feel isolated from others'. Higher scores indicate a higher level of loneliness. The original and Japanese version of UCLA was validated elsewhere.^{50 51}

Social isolation

A Japanese version of the Lubben Social Network Scale-6 (LSNS-6) was used to assess social isolation with five response options: 0=none, 1=one, 2=two, 3=three or four, 4=five thru eight, 5=nine or more.⁵² Each LSNS-6 question is scored on a 0 to 5 scale. The total score is the sum of all items, which ranges from 0 to 30. The three items asked about family networks and three items about non-family networks. Lower scores indicate a higher level of social isolation. The Japanese version of LSNS-6 was validated elsewhere.⁵³

Demographic variables

Gender (male/female), age (categorised: 15–29, 30–44, 45–59, >60), marital status (married/single), educational attainment (junior high school, high school; two-year college, bachelor's degree, master's or doctoral degree), annual household income (less than 3 million, 3–5, 5–8, 8–10, >10, unknown), people living with (no one/someone), living with a child (yes/no), work status (currently working, no paid work, student) and subjective health status (excellent, good, average, poor, very poor) were collected as demographic variables.

Statistical analysis

Analysis of variance was conducted to examine the difference in outcome variables by demographic variables. Analysis of covariance was performed to compare the difference in outcome variables by living conditions (lower urbanisation level and lower deprivation, higher urbanisation level and lower deprivation, lower urbanisation level and higher deprivation, higher urbanisation level and higher deprivation) while adjusting for gender, age, educational attainment, income, marital status, people living with, work status and subjective health status. The analysis was weighted by using sampling weights to adjust the difference between participants in this internet survey and national representative samples. A Bonferroni post hoc test was used to assess the significance of group difference. For sensitivity analysis, the same analysis stratified by gender. Statistical significance was set as a two sided $p < 0.05$. Analysis was done with SPSS V.28.0. Japanese version (IBM). Multilevel analysis was not conducted in the current study due to within-class correlations was low (less than 0.1 of the Intraclass Correlation Coefficient).⁵⁴

RESULTS

Among the whole sample of 31 000, after eliminating discrepancies and/or artificial/unnatural responses, and respondents with unavailable ADI information, 27 520

were included in this study. The participants' characteristics and mean scores of loneliness and social isolation are shown in [table 1](#). The mean age (SD) was 50.3 years old (17.0). The mean scores of loneliness (UCLA-LS3-SF3) and social isolation (LSNS-6) in the whole sample were 4.13 (SD=1.66) and 10.36 (SD=6.09), respectively. Greater loneliness was found in women, 30–44 years old, less than one million in income, single, living with no one, students, junior-high school degree and with very poor subjective health status, compared with counterparts. Greater social isolation (low social support, low scores of LSNS-6) was found in men, 45–59 years old, less than one million in income, single, living with no one, currently working, a junior-high school degree, and with very poor subjective health status, compared with counterparts.

[Table 2](#) shows the difference in mean scores for loneliness and social isolation compared with living conditions. For loneliness, higher urbanisation level and higher deprivation showed significant and highest scores in the crude model. But the significance disappeared after adjusting for individual demographic variables. Rather, lower urbanisation level and higher deprivation had the highest scores in the adjusted model. For social isolation, higher urbanisation level and higher deprivation were significant and had the lowest scores (high social isolation) in the crude model, and higher urbanisation level and lower deprivation in the adjusted model. Estimated mean of loneliness and social isolation divided by living conditions in the adjusted model are shown graphically in [figure 1](#). Higher urbanisation level and lower deprivation had a significant difference in social isolation with each of the other groups.

The results of sensitivity analysis stratified by gender are shown in online supplemental file 1. The significance in the adjusted model for social isolation shown in the main analysis remained for both men and women.

DISCUSSION

This study found that living in a highly urbanised area was significantly associated with high social isolation even after adjusting for personal characteristics. In comparison, there was no significance found for loneliness, although high loneliness was observed in a more deprived area in the crude model. Overall, the differences for loneliness and social isolation by living condition were small in Japan. Nevertheless, this study suggests the potential public health needs, especially in urban areas, for addressing social isolation during a pandemic.

Women, 30–44 years old, lower income, single, living alone, with low educational attainment, and with very poor health status showed greater loneliness. The results were in line with existing evidence about risk factors of loneliness,^{11–14} except for young age.^{30–44} In our data, elderly people (>60) had the lowest scores for loneliness. The same tendency was found in an online Japanese study,⁵⁵ which sampled respondents aged 13–80. The older respondents to an online survey may be more active and familiar with communication technology, resulting in less loneliness.^{56 57}

Table 1 Participant characteristics and mean scores of loneliness and social isolation (N=27 520)

| | N (%) | Loneliness (possible range 3–9) | | Social isolation* (possible range 0–30) | |
|--|---------------|------------------------------------|-------------------|--|-------------------|
| | | Mean (SD) | P for difference* | Mean (SD) | P for difference† |
| Gender | | | | | |
| Male | 13 525 (49.1) | 4.04 (1.62) | <0.001* | 9.85 (6.28) | <0.001* |
| Female | 13 995 (50.9) | 4.21 (1.70) | | 10.86 (5.86) | |
| Age | | | | | |
| 15–29 years old | 4036 (14.7) | 4.35 (1.78) | <0.001* | 11.58 (6.12) | <0.001* |
| 30–44 years old | 6546 (23.8) | 4.40 (1.83) | | 9.68 (5.79) | |
| 45–59 years old | 7481 (27.2) | 4.36 (1.78) | | 9.14 (5.92) | |
| Over 60 years old | 9457 (34.4) | 3.67 (1.25) | | 11.29 (6.17) | |
| Marital status | | | | | |
| Married | 16 610 (60.4) | 3.90 (1.46) | <0.001* | 10.96 (5.96) | <0.001* |
| Single | 10 910 (39.6) | 4.48 (1.87) | | 9.45 (6.17) | |
| Educational attainment | | | | | |
| Junior high school graduate | 376 (1.4) | 4.35 (1.93) | 0.006* | 8.90 (6.58) | <0.001* |
| High school graduate | 7598 (27.6) | 4.12 (1.66) | | 10.15 (6.20) | |
| Two-year college graduate | 6117 (22.2) | 4.18 (1.70) | | 10.46 (5.94) | |
| Bachelor’s degree | 12 070 (43.9) | 4.11 (1.64) | | 10.55 (6.07) | |
| Master’s or doctoral degree | 1359 (4.9) | 4.11 (1.65) | | 9.76 (6.11) | |
| Household income (million JPY/year) | | | | | |
| Less than 3 | 4763 (17.3) | 4.45 (1.87) | <0.001* | 8.98 (6.19) | <0.001* |
| 3 to less than 5 | 6040 (21.9) | 4.11 (1.65) | | 10.29 (5.90) | |
| 5 to less than 8 | 5959 (21.7) | 4.02 (1.55) | | 10.71 (5.80) | |
| 8 to less than 10 | 2372 (8.6) | 3.97 (1.49) | | 11.25 (5.95) | |
| 10 or more | 2544 (9.2) | 3.92 (1.48) | | 11.78 (6.13) | |
| No response/unknown | 5842 (21.2) | 4.15 (1.72) | | 10.23 (6.29) | |
| Living with | | | | | |
| No one (alone) | 5746 (20.9) | 4.40 (1.82) | <0.001* | 8.98 (6.16) | <0.001* |
| Someone | 21 774 (79.1) | 4.06 (1.61) | | 10.73 (6.02) | |
| Living with child/children | | | | | |
| No | 12 738 (46.3) | 4.12 (1.68) | 0.451 | 10.42 (6.08) | 0.171 |
| Yes | 14 782 (53.7) | 4.14 (1.65) | | 10.32 (6.10) | |
| Work status | | | | | |
| Currently working | 17 099 (62.1) | 4.14 (1.66) | <0.001* | 10.18 (6.01) | <0.001* |
| No paid work | 9196 (33.4) | 4.08 (1.65) | | 10.37 (6.20) | |
| Student | 1225 (4.5) | 4.34 (1.80) | | 12.81 (5.90) | |
| Subjective health status | | | | | |
| Excellent | 5484 (19.9) | 3.53 (1.17) | <0.001* | 12.39 (6.15) | <0.001* |
| Good | 9467 (34.4) | 3.86 (1.40) | | 11.13 (5.84) | |
| Average | 8651 (31.4) | 4.24 (1.65) | | 9.36 (5.84) | |
| Poor | 3186 (11.6) | 5.22 (2.02) | | 8.12 (5.74) | |
| Very poor | 732 (2.7) | 6.12 (2.44) | | 6.81 (6.24) | |

*p<0.05.

*Lower scores indicate a higher level of social isolation.

†Analysis of variance was conducted to test group difference.

Online surveys may lead to an underestimation of loneliness in elderly people. A Japanese governmental national survey, which recruited participants based on resident registration

data, also reported that severe loneliness was observed mostly in the 30s (7.9%) and least in the 70s (1.8%).⁵⁸ The result was contrary to a recent meta-analysis of European data

Table 2 Analysis of covariance divided by living conditions using urbanisation level and deprivation (N=27 520)

| | N | Crude | | Adjusted* | | | |
|--|------|-------|------|-----------------------------|----------------|------|-----------------------------|
| | | Mean | SD | F value, p value | Estimated mean | SE | F value, p value |
| Loneliness | | | | | | | |
| Lower urbanisation level and lower deprivation | 5483 | 4.09 | 1.63 | 6.266, p<0.001 [†] | 3.99 | 0.03 | 1.10, p=0.349 |
| Higher urbanisation level and lower deprivation | 8290 | 4.09 | 1.62 | | 3.99 | 0.03 | |
| Lower urbanisation level and higher deprivation | 8538 | 4.15 | 1.69 | | 4.01 | 0.02 | |
| Higher urbanisation level and higher deprivation | 5209 | 4.20 | 1.73 | | 3.94 | 0.03 | |
| Social isolation | | | | | | | |
| Lower urbanisation level and lower deprivation | 5483 | 10.58 | 6.09 | 4.302, p=0.005 [†] | 9.76 | 0.11 | 10.83, p<0.001 [†] |
| Higher urbanisation level and lower deprivation | 8290 | 10.32 | 6.07 | | 9.11 | 0.11 | |
| Lower urbanisation level and higher deprivation | 8538 | 10.39 | 6.14 | | 9.85 | 0.09 | |
| Higher urbanisation level and higher deprivation | 5209 | 10.16 | 6.04 | | 9.67 | 0.12 | |

Urbanisation level was defined by Densely Inhabited District (DID) data, which was divided into two groups (high or low). Deprivation was defined by Area Deprivation Index (ADI) data, which was divided into two groups (high or low).

[†]p<0.05.

*Adjusted by gender, age, educational attainment, income, marital status, people living with, work status and subjective health status, using sampling weights to adjust the difference between participants in this internet survey and national representative samples.

suggesting young and middle-aged adults had a low prevalence of loneliness compared with older adults.⁵⁹ Accordingly, the age pattern of loneliness might be context specific, and further investigation should be done in Japan.

Regarding social isolation, men, 45–59 years old, lower income, single, living alone, currently working, with low educational attainment and with very poor health

status showed greater social isolation. These findings partially coincided with recent reports done during the COVID-19 pandemic,^{60 61} suggesting that living alone, being middle-aged and a poor economic situation, are associated factors for social isolation. In Japan, men were more isolated even before the COVID-19 pandemic than women.^{15 16 62} A lower income and low educational

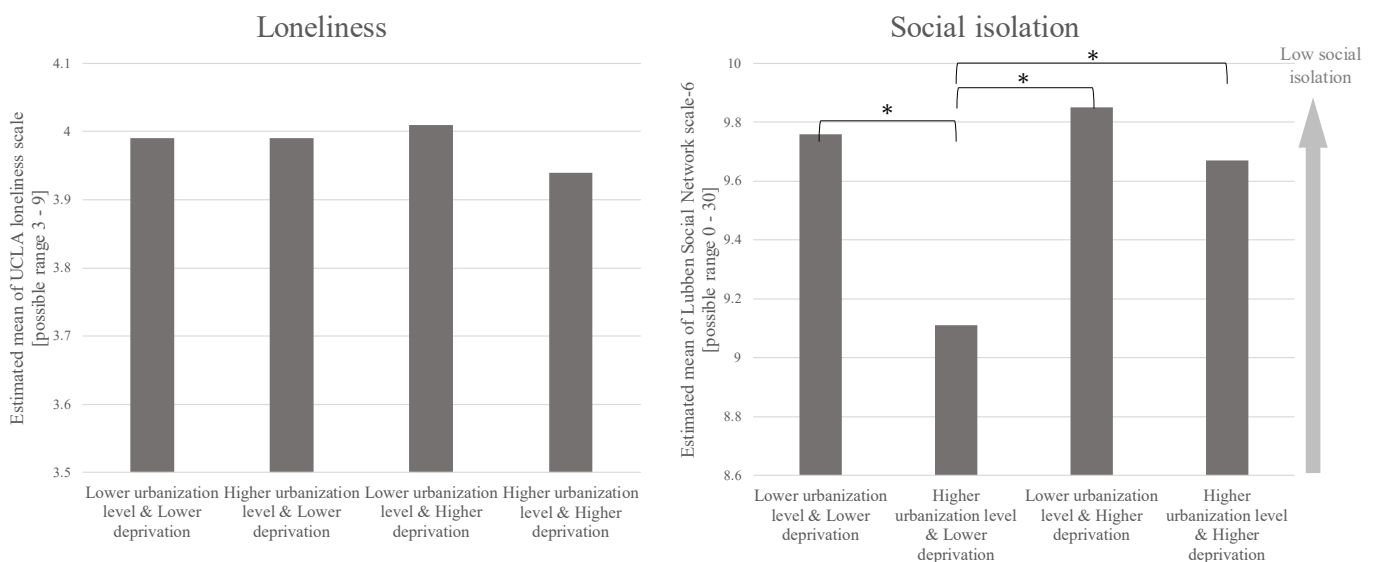


Figure 1 Estimated mean of loneliness and social isolation divided by living conditions in adjusted model. Note: Adjusted by gender, age, educational attainment, income, marital status, people living with, working status and subjective health status using sampling weights to adjust the difference between participants in this internet survey and national representative samples. UCLA, University of California, Los Angeles.

attainment are well-known risk factors of social isolation, reflecting disadvantages in obtaining social resources. Poor perception of health is also well-known associated factor of social isolation⁶³ because of less social participations. Although the working population and middle-aged people showed high isolation, this may be because the measurement scale does not include items about contact with colleagues (ie, work-related connections). Future study should consider various contacts to more accurately assess social isolation, especially if a middle-aged population is included in the sample.

For loneliness, living condition did not show a significant difference in the adjusted model. In the crude model, a higher deprivation level showed high loneliness. The tendencies for the highest score slightly changed between the crude and adjusted model, from higher urbanisation level and higher deprivation to lower urbanisation level and higher deprivation. This result was the same as a previous study showing that loneliness was greater in a highly deprived area, but no significance was found in an adjusted model.²⁹ Loneliness is not a static experience and easily fluctuates.⁶⁴ Moreover, its dynamic, complex and multidimensional characteristics make it difficult to understand individual loneliness from area-based perspectives.⁶⁵ Area-based loneliness (ie, 'I often feel lonely living in this area') was reported to be associated with deprivation, rather than individual loneliness.²⁹ A deprived area may reflect various features of an environment such as fewer community amenities, high crime rate or fewer opportunities to create trust with neighbours. The unavailability of social resources can promote loneliness. Loneliness has been associated with a meso-level and micro-level environment; for example, perceived good quality of a neighbourhood environment (eg, satisfaction with services, facilities and amenities),^{26 27 66} living nearby to hills or dangerous crossroads,⁶⁷ and living without green space^{68–70} may be stronger factors for loneliness than a macro-level environment, which was assessed in our study. Compared with urbanisation, deprivation may be a more important factor to that affects loneliness,²⁹ while individual basic characteristics (eg, married, income) strongly affect loneliness as established associated factors. In another study, people in rural areas may accept their geographical isolation but are not necessarily lonely.⁶⁰

For social isolation, living condition showed a significant difference, even after adjusting for individual background. Higher urbanisation level and lower deprivation had the highest scores. A previous Japanese study prior to the COVID-19 pandemic using the same measurement scale (N=2193) showed no significant association in social isolation among urbanity (large city, middle city, small municipality), which defined population size,¹⁹ but another study using another measurement scale showed a linear tendency where living in a high urbanisation area (defined by population density) showed a higher rate of social isolation during the COVID-19 pandemic.¹⁵ From the beginning of the pandemic, social isolation has increased worldwide.^{15 71}

People living in a high-density area may face greater challenges during a COVID-19 pandemic due to fewer opportunities to directly contact social networks, especially friends and family, because residents are sometimes living in an urban area away from their hometown. Since the measurement scale (LSNS-6) has two items asking about the opportunity to meet a friend and family member in person, the scores for people who live far from their friends and family can be necessarily low. Sensitivity analysis showed that living condition was associated with social isolation in both men and women. In both groups, higher urbanisation showed high social isolation, coinciding with previous studies.^{28 32 33}

Implications

Local public health policy and practice may need to address loneliness and isolation by implementing evidence-based interventions,⁷² particularly during a pandemic. This study has identified a potential high-priority area in this regard.

Limitations

There were several limitations in this study. First, this study applied a cross-sectional design, and we could not identify the causal relationship. Second, living condition was divided based on ADI and DID by using the cut-off of each median. A clinical or socially meaningful cut-off was not applied. Third, the online survey method contributed to several biases. Access to online surveys may have a selection bias, especially for an older population, although most of the Japanese population has access to the internet. Fourth, there might be uncontrolled confounding factors between living conditions and loneliness and isolation. While we used possible factors based on previous studies as covariates, the possibility that confounders exist cannot be denied. Loneliness and social isolation may be more affected by support from neighbourhoods or direct (face-to-face) communications. Such community resources (ie, micro-level environment) can possibly affect both characteristics of the living area and loneliness or isolation, but this was not considered in this study. Additionally, a meso-level environment (eg, hills, green space) was also not considered. Further study is needed to consider both meso-level accessibility and satisfaction for micro-level resources, not just using the indicator of urbanisation and deprivation. Finally, the influence of COVID-19 pandemic may affect the association between living condition and loneliness and social isolation. Knowledge about infectious measures and fully packed living condition may make people living in a higher urbanisation level and lower deprivation avoid social contacts, leading the results of the highest score for social isolation. Conducting the research at other times after the pandemic might yield different results.

CONCLUSION

This study aimed to investigate the association between living conditions (deprivation and urbanisation level) and loneliness and social isolation. Although the overall

findings found only a small effect of living conditions on loneliness and social isolation, there were also trends indicating that loneliness is exacerbated in more deprived areas and that increased urbanisation impacts social isolation. This study suggests the need to pay attention to the area characteristics in considering public health practice. Future study is needed to investigate the environmental factors affecting loneliness and isolation.

Correction notice This article has been corrected since it was first published to add missing funding information.

Contributors DN was responsible for the overall content as the guarantor, supervising the process, and providing his expert opinion on the subject. NS and TT organised the study design. The questionnaire was created through discussions with collaborators outside of this work. NS analysed the data. NS wrote the first draft of the manuscript. TT and RO revised the manuscript critically. All authors approved the final version of the manuscript.

Funding This study was supported by the Japan Society for the Promotion of Science (JSPS) KAKENHI Grants (grant number 21H04856, 19K10446, 18H03107), the Health Labour Sciences Research Grant (grant number 19FA1005; 19FA1012; 22FA2001; 22FA1010), Grants from Chiba Foundation for Health Promotion & Disease Prevention, Innovative Research Program on Suicide Countermeasures (R3-2-2), the Ministry of Health, Labour and Welfare (MHLW) Special Research Program Grant (grant number JPMH20CA2046), JST RISTEX grants (JPMJRX21K6) and the Japan Agency for Medical Research and Development (AMED; grant number 2033648).

Competing interests NS reports personal fees from Medilio Co., Ltd, outside the submitted work. DN reports personal fees from Startia, Inc., personal fees from en-power, Inc., personal fees from MD.net, outside the submitted work. The other authors have no conflicts of interest.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Online informed consent was obtained from all participants with full disclosure and explanation of the purpose and procedures of this study. The panellists had the option to not respond to any part of the questionnaire and the option to discontinue participation in the survey at any point.

Ethics approval The study was reviewed and approved by the Research Ethics Committee of the Osaka International Cancer Institute (number 20084 at 19 June 2020; number 20084-8 at 14 June 2022) and by the Research Ethics Committee of Graduate School of Medicine/Faculty of Medicine, The University of Tokyo (number 2020336NI-(2)). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. 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.

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