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Note

Detection of outlier prefectures on the mortality due to COVID-19 in Japan

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ABSTRACT

Japan has suffered from COVID-19 with significant mortality, but its prefectural differences are not well investigated. Since the mortality due to COVID-19 was likely to be associated with the number of infected cases, the population density, and the proportion of the elderly population, we tried to detect the outlier prefectures by multiple linear regression analyses. With the use of the Hampel identifier, we found that Hokkaido and Hyogo were the outlier prefectures with higher mortality after adjusting the variables above. Further studies should delineate the causes of these differences.

Note

Although the deaths associated with COVID-19 in western pacific nations such as Japan remain relatively low as of this writing [1], it resulted in more than 47,000 deaths in Japan by November 10, 2022 (data from the Ministry of Health, Labour, and Welfare of Japan. https://www.mhlw.go.jp/stf/covid-19/open-data.html Viewed, November 14, 2022). There appear to have significant regional differences in the cumulative mortality per population among prefectures of Japan, ranging from 75.4 deaths per 100,000 population in Osaka prefecture to 8.4 per 100,000 in Niigata. However, multiple factors could have influenced the difference. For example, the population density of any given region may be associated with mortality due to COVID-19 [2]. The proportion of elderly people also might influence their mortality [3,4]. In addition, the number of COVID-19 cases per population is likely to be associated with its mortality (Cumulative confirmed COVID-19 deaths vs. cases, Nov 12, 2022. https://ourworldindata.org/grapher/covid-19-cumulative-confirmed-cases-vs-confirmed-deaths In. One World in Data. Source: Johns Hopkins University CSSE COVID-19 data. Viewed, November 14, 2022).

Previous studies tried to describe the regional differences in COVID-19 epidemiology in Japan [5,6]. However, the prefectural differences in terms of mortality have not been well investigated, particularly on the outliers with significantly higher or lower mortality. Here, we investigated the prefectural mortality differences due to COVID-19 in Japan, focusing on detecting the outlier prefectures.

The linear regression analyses were conducted between the prefectural COVID-19 mortality and the following variables; 1) the population density, 2) the proportion of the people above the age of 65 years old, and 3) the cumulative number of infected people per 100,000 population. The COVID-19 data were derived from the Ministry of Health, Labour, and Wealth of Japan as of November 10, 2022, as described above. The data on the population density was derived from the Statistics Bureau of Japan as of October 1, 2021, and from the Geospatial Information Authority of Japan as of October 1, 2021 (https://www.stat.go.jp/data/jinsui/2021np/index.html and https://www.gsi.go.jp/ Viewed. May 1, 2022). The data on the proportion of people above the age of 65 years old was derived from the Cabinet Office data in 2018 (https://www8.cao.go.jp/kourei/whitepaper/w-2019/html/zenbun/s1_1_4.html Viewed, November 1, 2022).

On the correlation with the mortality per 100,000 population, Pearson's product-moment correlation coefficient were 0.48 for the population density ($p = 0.0006$, Fig. 1A), −0.39 for the proportion of the people above the age of 65 years old ($p = 0.006$, Fig. 1B), and 0.73 for the COVID-19 cases per 100,000 population ($p < 0.0001$, Fig. 1C). Multiple linear regression analysis showed the coefficients for the population density, the proportion of people over 65, and the COVID-19 cases of 0.0032, 1.28, and 0.0024 respectively ($p < 0.0001$, $p = 0.02$, and $p = 0.04$ respectively, Supplementary file. Section 1).

Hampel Identifier was used to detect the outlier prefectures [7]. The residuals appeared to follow the normal distribution (Supplementary file. Section 2). Median residuals after multiple linear regression analysis were −0.66 (range −15.34 to 21.90). Defining the outliers as the number above or below the standard deviation x 3, the upper and lower thresholds were calculated to be 16.83 and −17.15 respectively. Only

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Hokkaido and Hyogo prefectures were found to be the outliers above the threshold (21.90 and 17.82 respectively). There was no outlier below the threshold. The residuals of each prefecture were graphically shown in Fig. 2.

We found the outlier prefectures in COVID-19 mortality. Hokkaido prefecture was found to be the biggest outliner associated with the highest mortality after adjusting the population density, the proportion of elderly people, and the cases of COVID-19 per population, followed by Hyogo prefecture. There was no outlier prefecture associated with lower mortality. In other words, all prefectures except for Hokkaido and Hyogo remained within the expected range of mortality after adjusting the variables.

Uni-variate analysis can potentially detect outliers mistakingly. For example, Osaka prefecture appears to be an outlier simply conducting uni-variate analyses (Fig. 1A, B, and 1C). However, Osaka was not associated with higher mortality after the adjustment, with a residual of 15.27, which was below the upper limit of 15.83. Likewise, Okinawa prefecture appears as an outlier in Fig. 1A as the one associated with higher mortality, and the opposite in Fig. 1C. It did not belong to either of these after multiple regression analysis. After adjusting these factors, only Hokkaido and Hyogo were found to be outliers. The cause of these differences remains unknown. We did not find any specific reasons to make these two prefectures stand out, such as the vaccination rate or the number of physicians per population [8,9]. There might be differences in the ways the mortality is reported among prefectures, although we were not able to delineate it. We need to investigate further the reasons for these differences to improve our healthcare system in terms of the care of COVID-19 patients.

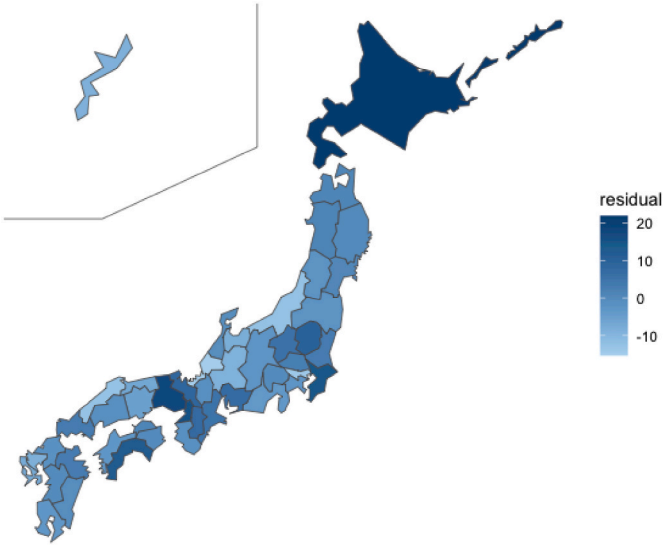

Fig. 2. The mapping of the residuals by the prefecture.

Our initial analysis revealed that the proportion of elderly people was inversely correlated with mortality, but the further multiple

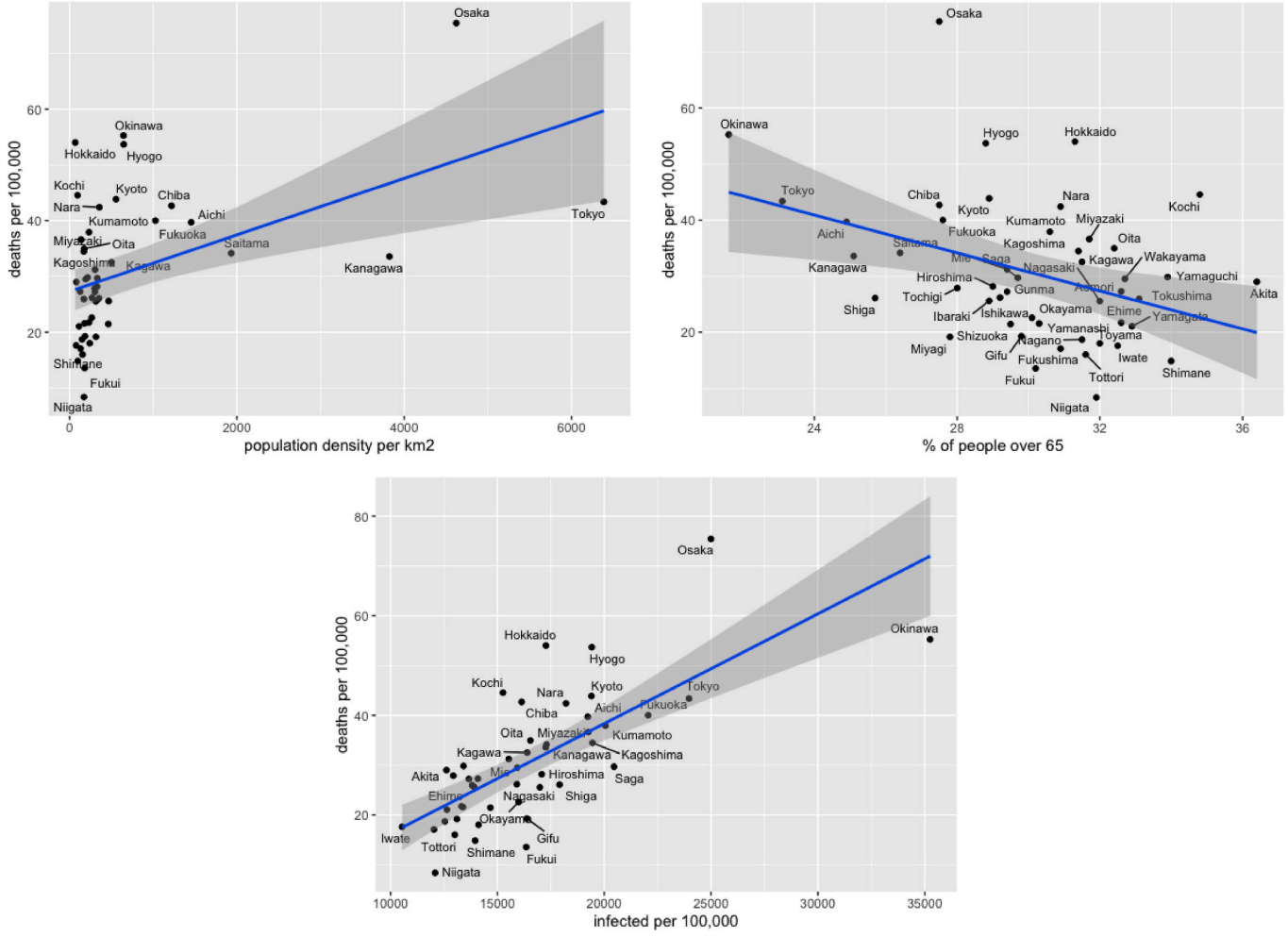

Fig. 1. The correlation with the mortality per 100,000 population, with the population density (A), the proportion of the people above the age of 65 years old (B), and the COVID-19 cases per 100,000 population (C).

regression analysis showed rather the opposite, most likely reflecting the presence of confounders since the proportion of the elderly tends to be higher in rural areas. The proportion of elderly people had the highest coefficient among the variables, suggesting the impact of having elderly people in the community is high in influencing COVID-19 mortality. It is not a surprising finding since older age was known to be associated with mortality due to COVID-19 by clinical studies [3]. This again underscores the importance of analysis by adjusting important variables.

Our study has several limitations. First, we preliminarily tried to identify the outlier prefectures by adjusting the potential confounders, but we might have not included other variables possibly associated with the outcome. For example, the capacity of the healthcare at any given prefecture might influence the outcome of COVID-19, but we did not include it in the analysis since the capacity has changed over time, and we found its evaluation rather difficult over time. Second, although we were able to see the prefectural differences, we were not able to evaluate intra-prefectural differences. Both Hokkaido and Hyogo are large prefectures with an area of 83,423.87 km^2 and 8400.94 km^2 respectively (Data from Geospatial Information Authority of Japan. https://www.gsi.go.jp/KOKUJYOHO/MENCHO-title.htm Viewed, November 16, 2022). Intra-prefectural variability is likely to exist in both prefectures, and our findings may not be generalized to each given region within these prefectures. We will need further studies to reveal intra-prefectural differences regarding identifying the factors associated with COVID-19 outcomes.

In conclusion, we identified the outlier prefectures which were associated with higher COVID-19 mortality. Further studies to elucidate its cause and the measures to improve the situation are needed.

Data availability

Data are available on the sites shown in the manuscript.

Contributors

Conception and the design of the study: KI and CM. The analysis of data: KI. Drafting of the manuscript: KI. The revision and the approval of the manuscript. All authors.

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Ethics statement

The current study is exempted from the ethics committee approval since the analysis was done using data from the public domain, there were no issues regarding the confidentiality of the patients, and there was no intervention provided for this study.

Declaration of competing interest

We have no conflicts of interest.

Acknowledgment

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jiac.2023.01.016.

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