PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of the COVID-19 pandemic on mortality trends in Japan: a reversal in 2021? A descriptive analysis of national mortality data, 1995-2021
AUTHORS	Tanaka, Hirokazu; Togawa, Kayo; Katanoda, Kota

VERSION 1 – REVIEW

REVIEWER	Black, Deborah The University of Sydney, Faculty of Medicine and Health
REVIEW RETURNED	19-Apr-2023

GENERAL COMMENTS	The abstract objective needs to state very clearly that it is looking at the impact of Covid-19 on Japan's ASMR.There are major limitations to the study. It is unsurprising that life expectancy went down in 2020 in countries where Covid-19 cases were high. There needs to be a table that lists the per capita Covid-19 cases in 2020 for a number of countries against the change in ASMR in 2020. The table should include both countries like Japan where Covid-19 cases were low as well as the countries listed in the this study. If there is a relationship between a general downward trend in overall ASMR in 2020 and low rates of Covid-19 and vice-versa, then what is the novelty in the results for 2020 for Japan? in summary, the objective of the study needs to be made clearer and relevant comparisons with outher countries need to be made.

REVIEWER	CHAN, Eunice The Chinese University of Hong Kong
REVIEW RETURNED	29-Apr-2023

GENERAL COMMENTS	This manuscript analyzes the Japanese age-standardized mortality rates from 1995 to 2021 using vital statistics. The authors investigated in the long-term mortality trends, focusing on the period of the COVID-19 pandemic in Japan. They calculated the cause-specific annual ASMR changes and summarized their findings. This study is important in understanding how the COVID-19 pandemic has affected the population health of Japan. Although Japan was not heavily affected by the COVID-19 pandemic with respect to the number of COVID-19 deaths, quarantine and lockdown protocols could have had (both positive and negative) effects on population health, such as reduction in mortality due to traffic accidents, increased morality due to delay in treatment. Therefore, I agree with the authors that further investigation and analysis for the mortality trends is needed.

	The authors did an excellent job in summarizing their findings. Their manuscript was extremely clear and easy to read. They were also able to highlight the important and interesting mortality trends, which could be beneficial when continuing this study for 2022. In their discussion, the authors were also able to provide plausible explanations for the reversal in mortality decline. The following is for the authors' consideration: - There are some minor typos, such as in the abstract conclusion, the "an" after "However" can be removed. - In your methodology, the 2015 Japan Standard Population was used; why was this one used? Is there a more current of the population? - Although some limitations were mentioned throughout the manuscript, it would be nice to have a section on the limitations of the study. - It would also be nice to understand what the MHLW definition of what it means to have "died of COVID-19". This may also explain the increase in mortality due to senility. - Is there a repository that we can access for the data and the analysis?

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Dr. Deborah Black, The University of Sydney
Comments to the Author:
The abstract objective needs to state very clearly that it is looking at the impact of Covid-19 on Japan's ASMR. There are major limitations to the study. It is unsurprising that life expectancy went down in 2020 in countries where Covid-19 cases were high. There needs to be a table that lists the per capita Covid-19 cases in 2020 for a number of countries against the change in ASMR in 2020. The table should include both countries like Japan where Covid-19 cases were low as well as the countries listed in the this study. If there is a relationship between a general downward trend in overall ASMR in 2020 and low rates of Covid-19 and vice-versa, then what is the novelty in the results for 2020 for Japan?
in summary, the objective of the study needs to be made clearer and relevant comparisons with other countries need to be made.

Response: Thank you for your comments. We have revised our paper accordingly. Please see our response below.

As you pointed out, life expectancy went down in many countries during the COVID-19 pandemic, while some other countries, including Japan, did not experience such a drop. In this study, we focused on the most recent trends in mortality in Japan, where the absolute number of COVID-19 cases was very small in 2020, but the annual number of reported COVID-19 cases increased rapidly in 2021 and 2022. We did not intend to discuss the COVID-19 pandemic and mortality in different countries, but aimed to present an example of emerging changes in mortality trends in a country seemingly less affected by COVID-19. We believe that this will appeal to international readers - namely that the increase in mortality occurred in 2021 for the first time since the advent of the COVID-

19 pandemic in one of the countries less affected by COVID-19 so far, in contrast to many other countries where the increase in mortality occurred in 2020 (e.g. U.S., France, and Italy).

To clarify our research questions and purposes, we have added some descriptions on the objective of our study (Abstract: line 38-41, Introduction: line 110-128). Also, in response to your suggestion we have made a new Figure 1 to show the changes in life expectancy between 2019 and 2020 for selected countries (for both sexes), and added related descriptions to the Methods (line 131-133) and Results sections (line 159-164). We believe that these changes will help readers understand the scope of our study.

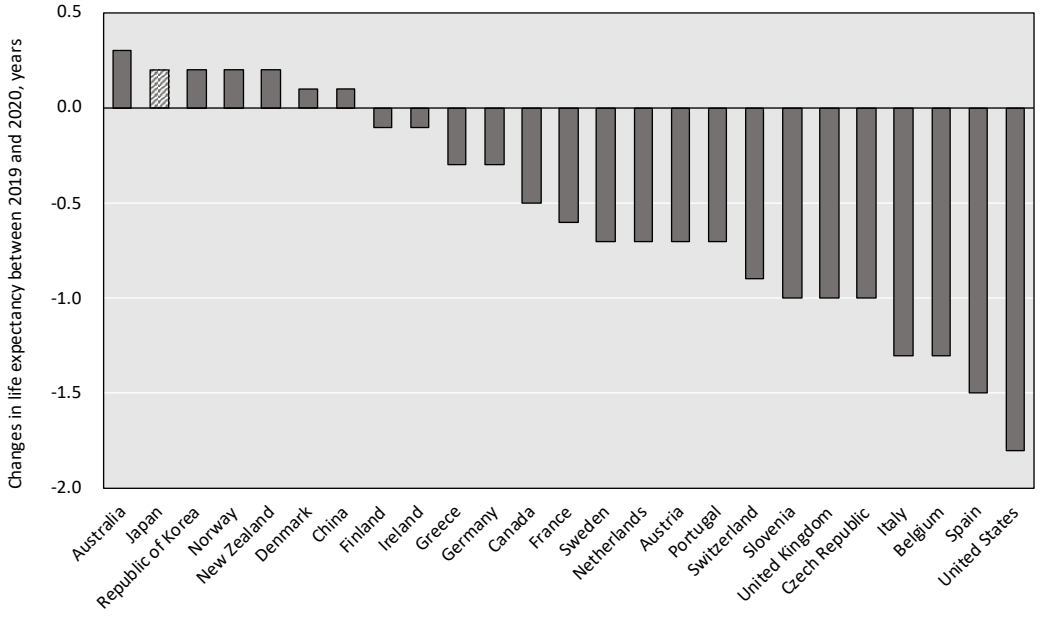

Figure 1. Changes in life expectancy between 2019 and 2020 for selected countries for both sexes

(line 38-41): Abstract

Objective: The COVID-19 pandemic led to an increase in mortality in most countries in 2020, deviating from prior decreasing trends. In Japan, however, mortality was suggested to decrease in 2020. This study investigated long-term mortality trends and cause-specific contributions, focusing on the period of the COVID-19 pandemic in Japan.

(line 110-128): Introduction

Approximately three years into the pandemic, the impact of COVID-19 on Japan continues to increase. Although the Japanese government did not introduce strict COVID-19 restrictions such as lockdown, people's daily lives were affected, as were the lives of health-care workers since the first declaration of a state of emergency in April 2020. To date, however, no nationwide mortality data that discuss the impact of the COVID-19 pandemic on mortality trends have been reported in Japan. Careful assessment of the impact of the pandemic on population health would aid in the evaluation of efforts during the pandemic and identify lessons, not only for Japan but also globally.

In most high-income countries, life expectancy in 2020 was shorter than that before, attributable to both the direct and indirect effects of COVID-19.[1] For example, reductions in life expectancy in 2020 were observed in Russia, the U.S., Spain, England/Wales, Netherlands, Sweden, and France.[2]

However, in Japan, life expectancy was not shortened in 2020 according to the Japanese Ministry of Health, Labour and Welfare (MHLW),[1,3] a deviation from the decreasing trend in most countries.[1]

Reasons for the prolonged life expectancy in 2020 despite the pandemic are unclear. One reason could be that Japan did not experience as large a number of COVID-19 cases that year as other countries. However, Japan experienced a six-fold increase in the number of reported cases from 2020 to 2021: 234 109 cases in 2020 and 1 492 874 cases in 2021.[4] Thus, annual mortality rate in 2021 in Japan may differ from the stable downward trend seen before 2020. This study aimed to explore the long-term mortality trends and cause-specific contributions during the COVID-19 pandemic in Japan, focusing on the years 2020 and 2021.

(line 131-139): Methods

We illustrated changes in life expectancy between 2019 and 2020 for selected countries, including Japan, using data extracted from the World Development Indicators managed by the World Bank.[1] To evaluate the trends in the number of COVID-19 cases in Japan, we extracted data on the daily number of reported COVID-19 cases from 16 January 2020 (the first case confirmed) to 1 January 2023 from Japanese government records.[4] The numbers of deaths (5-year age intervals) between 1995 and 2021 were extracted from the vital statistics (complete deaths record) in Japan managed by MHLW.[3] The 2021 complete mortality data were published in September 2022.[3] The vital statistics cover all Japanese deaths that occurred in Japan. The relevant population data were also collected from the vital statistics and population census.

(line 158-163): Results

Figure 1 shows Japan was one of the countries where life expectancy was prolonged in 2020 despite having shortened in many high-income countries such as the U.S. and France. Figure 2 shows trends in the daily number of reported COVID-19 cases in Japan since 16 January 2020. The peak of reported COVID-19 cases was observed in August 2022 (7th COVID-19 wave). While the absolute number of COVID-19 cases was very small in 2020, the annual number of reported COVID-19 cases increased rapidly in 2021 and 2022.

Reviewer: 2

Dr. Eunice CHAN, The Chinese University of Hong Kong
Comments to the Author:
This manuscript analyzes the Japanese age-standardized mortality rates from 1995 to 2021 using vital statistics. The authors investigated in the long-term mortality trends, focusing on the period of the COVID-19 pandemic in Japan. They calculated the cause-specific annual ASMR changes and summarized their findings.
This study is important in understanding how the COVID-19 pandemic has affected the population health of Japan. Although Japan was not heavily affected by the COVID-19 pandemic with respect to the number of COVID-19 deaths, quarantine and lockdown protocols could have had (both positive and negative) effects on population health, such as reduction in mortality due to traffic accidents, increased morality due to delay in treatment. Therefore, I agree with the authors that further investigation and analysis for the mortality trends is needed.
The authors did an excellent job in summarizing their findings. Their manuscript was extremely clear and easy to read. They were also able to highlight the important and interesting mortality trends, which could be beneficial when continuing this study for 2022. In their discussion, the authors were also able to provide plausible explanations for the reversal in mortality decline.

Response: We are grateful for your favorable comments. We have examined them carefully and revised our paper accordingly. Please see our responses below.

The following is for the authors' consideration:

- There are some minor typos, such as in the abstract conclusion, the "an" after "However" can be removed.

Response: Thank you. We have modified this sentence (Abstract).

- In your methodology, the 2015 Japan Standard Population was used; why was this one used? Is there a more current of the population?

Response: The 2015 Japan Standard Population is the latest version of standard population in Japan published in February 2022 by the Ministry of Health, Labour, and Welfare (MHLW). Our research group explained the detail and discussed the update effects recently. We added this statistical paper as a citation.

(new citation #5)

Tanaka H, Tanaka S, Togawa K, Katanoda K. Practical implications of the update to the 2015 Japan Standard Population: mortality archive from 1950 to 2020 in Japan. *J Epidemiol*. (in press) https://doi.org/10.2188/jea.JE20220302

- Although some limitations were mentioned throughout the manuscript, it would be nice to have a section on the limitations of the study.

Response: Thank you for your comment. Our finding suggested that the increase of COVID-19 cases may be associated with a mortality increase in 2021; however, further analysis is needed to clarify the quantitative impact of items such as ‘excess deaths.’ Also, long-term monitoring is necessary from 2022 onwards, especially for deaths from chronic diseases that may be subject to long-term effects by changes in lifestyle and medical care. We have added these descriptions in the Discussion section (Discussion: line 245-249).

(line 244-248): Discussion

This study is a descriptive analysis of national mortality data and should accordingly be interpreted with caution. Our findings suggest that the mortality increase in 2021 may be associated with the increase in COVID-19 cases; however, further analysis is needed to clarify the quantitative impact

such as ‘excess deaths’. Also, long-term monitoring is necessary from 2022 onwards, especially for deaths from chronic diseases that may have long-term effects by changes in lifestyle and medical care.

- It would also be nice to understand what the MHLW definition of what it means to have "died of COVID-19". This may also explain the increase in mortality due to senility.

Response: The Ministry of Health, Labour, and Welfare (MHLW) follows the algorithm for classifying the causes of death based on ICD-10. We have added a description of this to the methods (line 149). We do not think the increase in mortality from COVID-19 directly caused the increase in senility. During the COVID-19 pandemic, however, changes in patterns or places of medical care may have resulted in more physicians reporting senility as the cause of death, as discussed in the Discussion section (line 224-235).

(line 149): Methods

MHLW follows the algorithm for classifying the causes of death based on ICD-10.

(line 223-234): Discussion

A substantial increase in mortality due to senility has been occurring since the mid-2000s, independent of the pandemic. This can be interpreted as a result of the rapid aging of the Japanese population. Although we applied age-standardization for mortality analysis, the increase in the absolute number of deaths from senility, especially for the oldest old (85 years and over), resulted in an increase in ASMR. During the pandemic, however, changes in patterns or places of medical care may have resulted in more physicians reporting senility as the cause of death, especially deaths at home. Indeed, excess deaths from senility at home have been observed since May 2020.[11] As such, for the elderly, both direct and indirect death by COVID-19 may be miscoded to senility, which contributed to excess deaths in 2021. The sharp increase in deaths by ‘other causes not classified as major causes’ in 2021 (Figure 3) may have occurred by a similar mechanism. Therefore, our findings suggest that senility and ‘other causes not classified as major causes’ may largely represent the excess deaths in Japan during the pandemic. This may also include underdiagnosis and potential misclassification of causes of death.

- Is there a repository that we can access for the data and the analysis?

Response: We do not have a repository for the data or the analysis in this study, but detailed data can be found in the appendix figures and tables. Mortality data are available from a portal site for Japanese Government Statistics (e-Stat: https://www.e-stat.go.jp/) as follows.

(line 261-263): Data availability

Data availability

This study used the vital statistics data from a portal site for Japanese Government Statistics (e-Stat: https://www.e-stat.go.jp/), and data at an individual level were not used.