

Decision Letter (JCQ-2025-0009)

From:

To:

CC:

BCC:

Subject: Journal of Clinical Question - Decision on Manuscript ID JCQ-2025-0009

Body: 15-Apr-2025

Dear Dr Horita,

Manuscript ID JCQ-2025-0009 entitled "Impact of the COVID-19 Pandemic on Cancer Diagnosis and Resection in Japan" which you submitted to the Journal of Clinical Question, has been reviewed. The comments of the reviewer(s) are included at the bottom of this letter.

The reviewer(s) have recommended publication, but also suggest some revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript.

To submit your revised manuscript, follow the below steps.

1. Access to <https://mc.manuscriptcentral.com/jcq> and log into the site.
 2. Click "Author" at the top left of the screen at "Home" page.
 3. Click "Manuscripts with Decisions" on Author Dashboard page.
 4. Click "create a revision" on the manuscript you are going to revise.
 5. The system creates your revision manuscript form. Provide your comments about the revised points at the response field, fill in on each field step by step as same as you did for the original submission, and submit your revised manuscript.
- IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.
Your manuscript number has been appended to denote a revision.

You will be unable to make your revisions on the originally submitted version of the manuscript. Instead, revise your manuscript using a word processing program and save it on your computer. Please also highlight the changes to your manuscript within the document by using the track changes mode in MS Word or by using bold or colored text.

Once the revised manuscript is prepared, you can upload it and submit it through your Author Center.

When submitting your revised manuscript, you will be able to respond to the comments made by the reviewer(s) in the space provided. You can use this space to document any changes you make to the original manuscript. In order to expedite the processing of the revised manuscript, please be as specific as possible in your response to the reviewer(s).

IMPORTANT: Your original files are available to you when you upload your revised manuscript. Please delete any redundant files before completing the submission.

Because we are trying to facilitate timely publication of manuscripts submitted to the Journal of Clinical Question, your revised manuscript should be uploaded as soon as possible. If it is not possible for you to submit your revision in a reasonable amount of time, we may have to consider your paper as a new submission.

Once again, thank you for submitting your manuscript to the Journal of Clinical Question and I look forward to receiving your revision.

Sincerely,
Professor Richard Isaacs
Editor in Chief, Journal of Clinical Question
jcqeic@gleampub.com

[Editor's Comments]
Associate Editor
Comments to the Author:
(There are no comments.)

[Reviewer(s)' Comments]
Reviewer: 1

Comments to the Author

Throughout the manuscript, "cancer screenings and resections", but the study is about cancer diagnoses and resections.

Can the authors explain why this update of an earlier study does not include the same cancer sites?

The authors state that "each case was registered with the first treatment provided soon after the diagnosis". What constitutes soon? This is important because a proper analysis of treatment would include a time-to-event analysis rather than count. This is also important because cancer treatment guidelines were to increase neo-adjuvant treatment when possible. Are the authors underreporting surgeries conducted because treatment data is inadequate.

Why are the authors reporting yearly counts rather than monthly counts? Yearly numbers ignore the wide variation in monthly counts within a year. The authors conclude that post-2021, diagnoses and resections returned to usual levels. But many publications looking at monthly rates have demonstrated that some cancers returned to usual levels prior to the end of 2020 (including Japan (e.g., Fujita et al 2023)), which is more informative than yearly counts.

Rates are typically reported when examining time trends. Why are the authors reporting cancer case counts rather than cancer case rates? Are population numbers not available?

The methodology used by the authors has a very large limitation. The authors assume that only 2020 was affected by the pandemic. However, it is clear from the output that some cancer sites have not returned to their expected values based on pre-pandemic trends. In addition, the conclusions are that diagnoses and resections have decreased during 2020 and 2021, but that can only be determined graphically, not statistically from the method used by the authors. The authors should be using an interrupted time series approach where the pre-pandemic period serves to generate a counterfactual during the pandemic and post-pandemic period. This has commonly been used to evaluate the impact of the pandemic on cancer populations. Many tutorials are available which describe this procedure (e.g., Bernal et al, 2017). In addition, this cumulative difference in cases counts can be determined at the end of the study period with 95% CI generated through bootstrapping. The current method is not appropriate for determining how many cases are considered "undiagnosed" by the end of the study period.

The method for evaluating the impact of the pandemic on resections is inappropriate. The results are highly correlated because the percentage of individuals receiving surgery has changed very little during the pandemic. A time-to-event analysis is preferable (i.e., cumulative incidence and competing risk regression where death is a competing risk), because it can determine whether surgery was delayed or not, which is a much more sensitive analysis. In addition, non-surgical treatments would need to be analyzed as well. Resection counts can decrease, but if they decrease at the same rate as cancer cases diagnosed, then the issue is not surgeries being delayed but diagnoses being delayed, which are different sections of the cancer journey. In addition, recommendations during the pandemic were to introduce neo-adjuvant treatment when appropriate to delay surgery. If delays in surgery are occurring without a corresponding shorter time to non-surgical treatments, that is a problem. If delays occur because neo-adjuvant treatment was provided, that is following guidelines and describes a very different image than what is presented by the authors.

In the discussion section, the authors once again refer to cancer screening. However, the authors now reference elective surgeries. Most cancer surgeries are not considered elective (e.g., breast reconstructive surgery is considered elective, but a mastectomy is not considered elective surgery).

Much of the discussion section needs to be adjusted. The authors are incorrectly describing the cancer treatment environment during the pandemic. The authors are stating that surgical oncologists had to consider "rationing" cancer surgeries, which is not the case. The recommendations cited in the manuscript were to introduce neo-adjuvant treatment to delay surgery when it was deemed appropriate, as opposed to not offering surgery. There is no mention of neo-adjuvant treatment by the authors. Some studies evaluating the time to treatment in cancer have concluded that most patients received treatment at the same rate as before the pandemic: only a small minority of sites had delayed surgeries, which were associated with an increase in neo-adjuvant treatment.

The authors give the impression that the pandemic was very disruptive in Japan. However, this study is an update of "Impact of the COVID-19 pandemic on cancer diagnosis and resection in a COVID-19 low-burden country: Nationwide registration study in Japan" which suggests that the pandemic was not very disruptive in Japan. It would be useful to cite studies from other countries and their diagnosis/treatment results along with their COVID rates to provide context and justify the language used in the manuscript. Presumably countries with high COVID rates would be more disrupted than countries with lower COVID rates (assuming accurate COVID data).

The authors state that "Although the impact of delays on cancer recurrence and survival rates ... these delays are expected to have a significant effect on cancer-related mortality rates". This statement is incorrect and it's unclear what the authors intend to indicate (e.g., delays on cancer diagnosis and/or treatment can lead to poorer survival, but this effect may not be apparent for several years).

It's unclear what a "resurgence" of diagnoses and surgeries represent. The numbers have increased, but a key result not presented is the cumulative difference at the end of the study period which indicates how concerned we should be about the decrease occurring during the pandemic (i.e., if the increase does not make up for the drop, then people should be concerned; if the increase makes up the drop, then people should not be concerned).

Reviewer: 2

Comments to the Author

This paper is the result of an analysis of the number of cancer diagnoses and resections in Japan during the COVID-19 pandemic.

This is a very short original paper, and the analysis merely lists the number of cases and resections each year from the hospital-based cancer registry. Similar results have been reported during this pandemic period worldwide. Such a short paper would still be understandable if reported during a pandemic.

However, it must be said that it lacks novelty in that it reports result with such little content as of 2025. Scientific papers are meant to communicate new findings to the reader, and that is what is decidedly lacking.

Reviewer: 3

Comments to the Author

Overall comment :

The article feels quite brief and lacks crucial details and contextual information that would allow the reader to fully assess its overall quality and contribution.

Method :

The methods section lacks sufficient detail about the model used. While it is stated that a linear regression was employed, important elements are missing—such as the controls included, model specifications, and key assumptions. For instance, were standard errors clustered at any administrative level? Were the data aggregated daily, monthly, or annually? Was the dependent variable log-transformed or otherwise modified? I would strongly encourage the authors to clearly specify the model, ideally in mathematical form, either in the main text or in supplementary materials, to allow for a proper evaluation of the analysis conducted.

The type of analysis conducted using the model needs to be explained more clearly. For example, why was fiscal year 2020 excluded? From what I understand, it appears that previous years may have been used to predict the outcome for 2020, which was then compared with the observed value—but since this is not clearly stated, it's difficult to be certain. Please clarify the analytical approach and provide a more detailed mathematical description, at least in the Appendix.

Additionally, the exclusion of fiscal year 2020 (starting in April 2020) should be more thoroughly justified. Was this due to the onset of COVID-19 in Japan at that time, or does it relate to limitations in the data aggregation (e.g., annual reporting)? A more explicit explanation would strengthen the credibility and transparency of the analysis.

Result :

Similar to the methods section, this part of the paper lacks essential detail regarding the models applied. It is crucial to include a table presenting the regression results, including the list of variables used, the R-squared value, and the number of observations. This information is fundamental for assessing the robustness and relevance of the findings.

Discussion:

It is unclear what period you are referring to when mentioning the "post-pandemic" phase—does this refer to 2021, 2022, or another period? You mention a resurgence in both diagnoses and surgical cases following the pandemic, but it is not clear how this effect was identified or measured. This should be clearly defined and described in the methods section.

Furthermore, the discussion of your results would benefit from greater depth, particularly in terms of their implications. Currently, the manuscript lacks international comparisons, which would provide valuable context. I recommend expanding the introduction to better situate the study within the national and international context, and incorporating a more detailed discussion comparing your findings with those of other countries. This would help highlight the significance and relevance of your results.

Conclusion:

The term "severe" impact of COVID-19 should be clearly defined. What is your criterion for assessing severity? Using objective measures—such as the reported 9.3% deviation in prostate cancer diagnoses—would be more appropriate than relying on subjective language. An international comparison, as suggested earlier, could also help contextualize whether the impact observed in your study was greater or lesser than in other countries.

Additionally, you mention the long-term consequences of the pandemic on cancer care, but this important point is only briefly addressed in the conclusion. It would be more effective to introduce this idea earlier in the manuscript and elaborate on it further in both the introduction and discussion sections, to strengthen the narrative and underscore the broader significance of your findings.

Date Sent: 15-Apr-2025

Author's Response to Decision Letter for (JCQ-2025-0009)

Impact of the COVID-19 Pandemic on Cancer Diagnosis and Resection in Japan

May 5th, 2025

Dr. Eduardo Guimarães Hourneaux de Moura

Journal of Clinical Question

Dear Dr. Moura,

We appreciate your detailed review of our manuscript, "Impact of the COVID-19 Pandemic on Cancer Diagnosis and Resection in Japan". We have carefully considered and replied for all of the comments by reviewers. We believe the revised manuscript has been strengthened and hope that you will now consider it suitable for publication in Journal of Clinical Question. Our detailed responses to the comments are as below.

[Reviewer(s)' Comments]

Reviewer: 1

Comments to the Author

Throughout the manuscript, "cancer screenings and resections", but the study is about cancer diagnoses and resections.

Thank you for the comment. We changed the study to only about the diagnoses and the text will be fixed.

Can the authors explain why this update of an earlier study does not include the same cancer sites?

Thank you for the comment. We included the cancer of early studies.

The authors state that "each case was registered with the first treatment provided soon after the diagnosis". What constitutes soon? This is important because a proper analysis of treatment would include a time-to-event analysis rather than count. This is also important because cancer treatment guidelines were to increase neo-adjuvant treatment when possible. Are the authors underreporting surgeries conducted because treatment data is inadequate

We appreciate your comment. We understand the limitation set on our current study because of the introduction of neo-adjuvant treatment. Due to limitations in the registry data, which do not provide detailed information on treatment timing or type, we decided not to perform an in-depth analysis of treatment patterns.

Why are the authors reporting yearly counts rather than monthly counts? Yearly numbers ignore the wide variation in monthly counts within a year. The authors conclude that post-2021, diagnoses and resections returned to usual levels. But many publications looking at monthly rates have demonstrated that some cancers returned to usual levels prior to the end of 2020 (including Japan (e.g., Fujita et al 2023)), which is more informative than yearly counts.

We understand your concern and the lack of accuracy of yearly analysis. However, in this case, since the analysis is conducted on a yearly basis and there is only a single data point for the COVID-19 period, the registry data are insufficient to perform a valid ITS analysis.

Rates are typically reported when examining time trends. Why are the authors reporting cancer case counts rather than cancer case rates? Are population numbers not available?

We appreciate this important point. We understand that reporting incidence per 100,000 population is a standard practice in epidemiology and has its value. However, we decided not to perform the analysis since the data were limited to patients from participating hospitals and while these institutions cover the majority of core hospitals in Japan, using the total Japanese population as the denominator would be inappropriate.

The methodology used by the authors has a very large limitation. The authors assume that only 2020 was affected by the pandemic. However, it is clear from the output that some cancer sites have not returned to their expected values based on pre-pandemic trends.

Thank you for your thoughtful comment. We fully understand the concern that some cancer sites may not have returned to pre-pandemic trends even after 2020. However, in Japan, national cancer screening programs resumed to near-normal levels starting in fiscal year 2021. Based on this recovery, we designated fiscal year 2020 (April 2020 to March 2021) as the primary “pandemic year” for the purpose of this analysis.

In addition, the conclusions are that diagnoses and resections have decreased during 2020 and 2021, but that can only be determined graphically, not statistically from the method used by the authors. The authors should be using an interrupted time series approach where the pre-pandemic period serves to generate a counterfactual during the pandemic and post-pandemic period. This has commonly been used to evaluate the impact of the pandemic on cancer populations. Many tutorials are available which describe this procedure (e.g., Bernal et al, 2017). In addition, this cumulative difference in cases counts can be determined at the end of the study period with 95% CI generated through bootstrapping. The current method is not appropriate for determining how many cases are considered “undiagnosed” by the end of the study period.

We appreciate this important point. However, interrupted time series (ITS) analysis requires a sufficient number of data points within each segment and for our study, only a single data point was available for the pandemic period due to the use of annual data.

The method for evaluating the impact of the pandemic on resections is inappropriate. The results are highly correlated because the percentage of individuals receiving surgery has changed very little during the pandemic. A time-to-event analysis is preferable (i.e., cumulative incidence and competing risk regression where death is a competing risk), because it can determine whether surgery was delayed or not, which is a much more sensitive analysis. In addition, non-surgical treatments would need to be analyzed as well. Resection counts can decrease, but if they decrease at the same rate as cancer cases diagnosed, then the issue is not surgeries being delayed but diagnoses being delayed, which are different sections of the cancer journey. In addition, recommendations during the pandemic were to introduce neo-adjuvant treatment when appropriate to delay surgery. If delays in surgery are occurring without a corresponding shorter time to non-surgical treatments, that is a problem. If delays occur because neo-adjuvant treatment was provided, that is following guidelines and describes a very different image than what is presented by the authors.

Thank you for the comment. We understand the limitation set on our current study because of the introduction of neo-adjuvant treatment. Due to limitations in the registry data, which do not provide detailed information on treatment timing or type, we decided not to perform an in-depth analysis of treatment patterns.

In the discussion section, the authors once again refer to cancer screening. However, the authors now reference elective surgeries. Most cancer surgeries are not considered elective (e.g., breast reconstructive surgery is considered elective, but a mastectomy is not considered elective surgery).

Thank you for the comment. We will delete reference to elective surgeries completely.

Much of the discussion section needs to be adjusted. The authors are incorrectly describing the cancer treatment environment during the pandemic. The authors are stating that surgical oncologists had to consider “rationing” cancer surgeries, which is not the case. The recommendations cited in the manuscript were to introduce neo-adjuvant treatment to delay surgery when it was deemed appropriate, as opposed to not offering surgery. There is no mention of neo-adjuvant treatment by the authors. Some studies evaluating the time to treatment in cancer have concluded that most patients received treatment at the same rate as before the pandemic: only a small minority of sites had delayed surgeries, which were associated with an increase in neo-adjuvant treatment.

Thank you for this important comment. We agree that our original discussion may have overstated the impact on cancer treatments. We have decided to focus the analysis and discussion solely on cancer diagnosis given the limitations of the original data.

The authors give the impression that the pandemic was very disruptive in Japan. However, this study is an update of “Impact of the COVID-19 pandemic on cancer diagnosis and resection in a COVID-19 low-burden country: Nationwide registration study in Japan” which suggests that the pandemic was not very disruptive in Japan. It would be useful to cite studies from other countries and their diagnosis/treatment results along with their COVID rates to provide context and justify the language used in the manuscript. Presumably countries with high COVID rates would be more disrupted than countries with lower COVID rates (assuming accurate COVID data).

Thank you for the important suggestion. We will correct the text and include the comparisons with other countries with high rates of COVID.

The authors state that “Although the impact of delays on cancer recurrence and survival rates ... these delays are expected to have a significant effect on cancer-related mortality rates”. This statement is incorrect and it’s unclear what the authors intend to indicate (e.g., delays on cancer diagnosis and/or treatment can lead to poorer survival, but this effect may not be apparent for several years).

We fully agree that the statement was confusing and inaccurate. We will improve the sentence to provide with better context.

It's unclear what a "resurgence" of diagnoses and surgeries represent. The numbers have increased, but a key result not presented is the cumulative difference at the end of the study period which indicates how concerned we should be about the decrease occurring during the pandemic (i.e., if the increase does not make up for the drop, then people should be concerned; if the increase makes up the drop, then people should not be concerned).

We understand that the reviewer is likely pointing out the lack of a direct comparison between the COVID-19 and post-COVID-19 periods. However, our analysis was based on the assumption of a continuous linear trend spanning before and after the COVID-19 periods, and we evaluated whether the COVID-19 period represented a deviation from this trend. Therefore, the post-COVID-19 resurgence was also incorporated into our evaluation.

Reviewer: 2

Comments to the Author

This paper is the result of an analysis of the number of cancer diagnoses and resections in Japan during the COVID-19 pandemic.

This is a very short original paper, and the analysis merely lists the number of cases and resections each year from the hospital-based cancer registry. Similar results have been reported during this pandemic period worldwide. Such a short paper would still be understandable if reported during a pandemic. However, it must be said that it lacks novelty in that it reports results with such little content as of 2025. Scientific papers are meant to communicate new findings to the reader, and that is what is decidedly lacking.

Thank you for your comment. We understand the concern regarding the limited novelty of our study, particularly given the number of similar reports published earlier in the pandemic. However, we believe our study still provides value by evaluating long-term trends and an updating picture of the effect of the pandemic on cancer care. We will refocus the scope on cancer diagnosis.

Reviewer: 3

Comments to the Author

Overall comment :

The article feels quite brief and lacks crucial details and contextual information that would allow the reader to fully assess its overall quality and contribution.

Method :

The methods section lacks sufficient detail about the model used. While it is stated that a linear regression was employed, important elements are missing—such as the controls included, model specifications, and key assumptions. For instance, were standard errors clustered at any administrative level? Were the data aggregated daily, monthly, or annually? Was the dependent variable log-transformed or otherwise modified? I would strongly encourage the authors to clearly specify the model, ideally in mathematical form, either in the main text or in supplementary materials, to allow for a proper evaluation of the analysis conducted.

Thank you for this important point. We specified the details of the conducted analysis including controls, model specifications, and key assumptions. The standard errors were not clustered since our only interest was in nationwide trends, and no transformation was applied since increase in case counts was rather modest.

The type of analysis conducted using the model needs to be explained more clearly. For example, why was fiscal year 2020 excluded? From what I understand, it appears that previous years may have been used to predict the outcome for 2020, which was then compared with the observed value—but since this is not clearly stated, it's difficult to be certain. Please clarify the analytical approach and provide a more detailed mathematical description, at least in the Appendix.

We understand your concern and we added the detail of the analysis in the table. We fitted a linear regression model using data from the non-COVID-19 periods and assessed whether the observed deviations during the COVID-19 period were statistically significant by performing a z-test based on the standard error of the regression.

Additionally, the exclusion of fiscal year 2020 (starting in April 2020) should be more thoroughly justified. Was this due to the onset of COVID-19 in Japan at that time, or does it relate to limitations in the data aggregation (e.g., annual reporting)? A more explicit explanation would strengthen the credibility and transparency of the analysis.

Thank you for the comment. We are happy to add description of how fiscal year was defined in the method section.

Result :

Similar to the methods section, this part of the paper lacks essential detail regarding the models applied. It is crucial to include a table presenting the regression results, including the list of variables used, the R-squared value, and the number of observations. This information is fundamental for assessing the robustness and relevance of the findings.

Thank you for the important suggestion. We understand that our description of both method and result was not enough and added the necessary details.

Discussion:

It is unclear what period you are referring to when mentioning the "post-pandemic" phase—does this refer to 2021, 2022, or another period? You mention a resurgence in both diagnoses and surgical cases following the pandemic, but it is not clear how this effect was identified or measured. This should be clearly defined and described in the methods section.

We understand your concern. We will clarify the definition of post-pandemic phase and clearly describe how we analyzed resurgence in our method section.

Furthermore, the discussion of your results would benefit from greater depth, particularly in terms of their implications. Currently, the manuscript lacks international comparisons, which would provide valuable context. I recommend expanding the introduction to better situate the study within the national and international context, and incorporating a more detailed discussion comparing your findings with those of other countries. This would help highlight the significance and relevance of your results.

Thank you for this comment. We added comparison with other countries in our discussion section.

Conclusion:

The term "severe" impact of COVID-19 should be clearly defined. What is your criterion for assessing severity? Using objective measures—such as the reported 9.3% deviation in prostate cancer diagnoses—would be more appropriate than relying on subjective language. An international comparison, as suggested earlier, could also help contextualize whether the impact observed in your study was greater or lesser than in other countries.

Thank you for this comment. We deleted the term "severe" and added comparison with other countries for clarification.

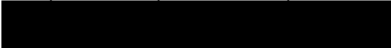
Additionally, you mention the long-term consequences of the pandemic on cancer care, but this important point is only briefly addressed in the conclusion. It would be more effective to introduce this idea earlier in the manuscript and elaborate on it further in both the introduction and discussion sections, to strengthen the narrative and underscore the broader significance of your findings.

Thank you for the crucial comment. We will expand the discussion of the long-term consequences both in introduction and discussion section in order to highlight the possibility of long-term implications.

As noted above, we believe this manuscript has been improved by the discussion suggested by the Reviewers. We hope the revised manuscript is now suitable for publication in Journal of Clinical Question.

Sincerely,

Nobuyuki Horita, M.D., Ph.D.
Chemotherapy Center
Yokohama City University Hospital
3-9, Fukuura, Kanazawa, Yokohama 236-0004, Japan



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