Peer Review File

Article information: https://dx.doi.org/10.21037/ajo-23-46

## Reviewer A

This study reviews the change in reported incidence of Head and Neck cancers in Victoria through the covid pandemic.

As the most locked-down area in the world, it is important to understand the impact of the lockdown.

This study is an important addition to the literature.

## Reviewer B

A good epi surgery paper of effects of difficulty in health care access in cancer diagnosis.

A good follow up given the group have access to the data would be:

- cancer stage based numbers )ie was treatment upstaged
- was access to surgery affected by limitation on diagnostic and therapeutic procedures (e.g. were T1 larynx scc treated with RT due to perceived risk of airway surgery on staff and limited access to OT, same issues with TORS)
- effect on DFS and OS at 3 year mark

## Editorial Comments

We thank the authors for submitting this great manuscript to our journal. This manuscript summarizes the association between the rates of newly diagnosed head and neck cancer and the COVID-19 pandemic and the corresponding lockdown measures in Victoria. Overall, the topic is interesting. However, there are some issues that need to be addressed, especially the data and the details of methods and results. The following are some suggestions:

# Major concerns:

Comment 1. Abstract-Background: We suggest the authors describe the study's objective (you could report "The objective of this study is to...").

**Reply 1**: Study objective has been added to the abstract-backgrounds see the revised abstract-background line 56

**Changes in text**: *The objective of this study is to evaluate the impact of COVID-19 related lockdown measures have had on the rate of new diagnosis of head and neck cancer*

2. Abstract-Results:

(1) "Based on expected calculations, there was a substantial drop in 2020 for cancers of the oral cavity, gums, oropharynx, nasopharynx, nasal cavity/sinuses, and larynx."

Authors should report the specific data, e.g., SIR, 95% CI, etc.

**Reply**: We have revised the sentence to include specific data.

**Changes in text**: *Statistically significant reductions from 2019 to 2020 being in tongue [SIR 87.0 (95% CI:76.5-98.9)] salivary gland [SIR 71.3 (95% CI: 56.5 – 90)].*

(2) "there was a substantial drop in 2020 for cancers of the oral cavity, gums, oropharynx, nasopharynx, nasal cavity/sinuses, and larynx." The word 'substantial' is somewhat of an exaggeration, because for some cancers, the drop was not significant, such as gum (95% CI: 60.9-112.3), oropharynx (95% CI: 82.1-109.7), etc. We suggest the authors delete the word 'substantial' or revise this sentence.

**Reply**: This sentence has been revised to remove the word substantial and include the specific sites with statistically significant reductions
**Changes in text:** *there was a decline in 2020 for cancers of the oral cavity, gums, oropharynx, nasopharynx, nasal cavity/sinuses, and larynx. Statistically significant reductions from 2019 to 2020 being in tongue [SIR 87.0 (95% CI:76.5-98.9)] salivary gland [SIR 71.3 (95% CI: 56.5 – 90)].*

(3) "This reduction was particularly prominent during quarter 2 and 3 periods where it corresponds with the highest restrictions", but in the Results (Lines 204-206), it is quarter 2 ("Oral cavity when analysed shown in figure 3 again demonstrates a similar trend to the overall head and neck data with a statistically significant reduction during quarter 2 which coincides with the initial lockdown period in Victoria").

**Reply**: Revised sentence to only include quarter 2.
**Changes in text:** This reduction was particularly prominent during quarter 2 period where it corresponds with the highest restrictions

3. Abstract-Conclusion: "The observed decrease in the incidence of HNC detected in Victoria corresponds to the COVID-19 pandemic peak incidence and public health response actions". This sentence is not rigorous because data on the peak incidence of the COVID-19 pandemic were not reported in the text.

**Reply**: sentence has been revised to remove 'peak incidence from sentence'
**Changes in text:** '*public health response actions to the COVID-19 pandemic'*

4. Methods:
(1) We suggest the authors reorganize the Methods section into several sections with subheadings (e.g., Participants, Data measurement, Statistical analysis, etc.).

**Reply**: Additional subheading of participants has been included
**Changes in text:** Addition of participant subheading

(2) Were there any missing data? If not, please kindly report it in the text.

**Reply:** The Victorian Cancer Registry is a population-based cancer registry. Under the legislation Improving Cancer Outcomes Act 2014, it is mandatory for health services, including pathology laboratories in Victoria to report to us all cancer diagnoses. On receiving the cancer information, the data is collated in person and tumour streams ensuring information is up-to-date and complete. Quality of data capture in registries is often measured by the percentage of cases for which only a death certificate exists, which is 0.4% in H&N cases in the VCR in 2021, which is among the lowest world-wide.
**Changes in text**: Nil

(3) How was such a large amount of data extracted? Was there a team of trained professionals? Was there any automated tool available?

**Reply**: Case level data was extracted from the population based Victorian Cancer Registry. The Victorian Cancer Registry receives pathology, hospital and other notifications that are consolidated into tumours and coded by professional medical coders.
**Changes in text:** Nil

(4) The database contains 254 hospitals and 26 pathology laboratories. Will there be any overlap between hospital and pathology laboratory samples? What if it overlaps?

**Reply:** Yes, most cases have both pathology and hospital notifications, and often more than one of each. As mentioned before, the VCR consolidates notifications into tumours and it is this consolidated data we used for the analyses.
**Changes in text:** Nil

(5) Why not use the date when the WHO declared the COVID-19 pandemic as a major public health event as the cut-off point (probably in February 2020)? That might be more convincing.

**Reply**: The dates that have been selected are to reflect the lockdown measures in Melbourne as this was when the restrictive measures were in place.
**Changes in text:**

5. Results:
(1) The description in the results section is a bit confusing. It is recommended that the authors add subheadings to provide a hierarchical description.

**Reply**: Additional subheadings have been used to provide clarity

**Changes in text**: See addition subheadings of *Overall head and neck cancers, oral cavity and oropharyngeal sites.*

(2) We strongly suggest that the authors mark the significant results in Table 1 with asterisks (e.g., Lip, Tongue, Salivary glands, etc.), so that readers can more easily understand why they were discussed in the results below.

**Reply**: Table 1 has been revised to add in asterisks for significant results
**Changes in text**: See Revised Table 1

(3) Do not report "statistically significant" simply because the data is greater than an arbitrary value. Please report the specific data, e.g., SIR, 95% CI, etc.

**Reply:** Specific data has been added in to sentences in which they have been described
**Changes in text**: Data added into

(4) Line 195-197: "Head and neck cancer ... (SIR = 95 [95%CI 88-101])", but in Table 1, it is "SIR = -56 [95%CI 89.7-100.9]".
Line 211: "Cancers of the lip increased from 164 in the year 2019...". But in Table 1, it is 169.
Line 212: "... (SIR = 121 [95%CI 106-139)." But in Table 1, it is "SIR = 36 [95%CI 105.9-139.3".
Line 214: "... (SIR = 121 [95% CI 87-169])." But in Table 1, it is "SIR = 6 [95% CI 86.9-168.6]".
Besides, we suggest the authors assign these results in one paragraph and cite Table 1.

**Reply**: There was a formatting error in this table which had the headings in the wrong position hence then having errors in the demonstration of data
**Changes in text**: Table 1 has been revised to reflect the accurate data reporting

(5) Lines 195-197: "Head and neck cancer cases in 2020 were expected to increase to 1167, approximately 3% up from 2019. In 2020, 1111 new diagnoses were observed...".
But in Table 1, the data is the opposite, the Observed column is 1167 and the Expected column is 1111. Besides, the totals of the Observed and Expected columns in Table 1 are also not 1167 and 1111.

**Reply**: As per the previous comment the Table 1 had been incorrectly formatted and has been revised to accurately reflect the results
**Changes in text**: Please see revised Table 1

(6) Lines 202-203: "Oral cavity and oropharyngeal subsites were the most common reported cases in the data overall, these demonstrated a reduction in observed rates (Figure 3)". This result cannot be derived from Figure 3, and authors are suggested to be cautious with their descriptions.

**Reply**: The sentence has been revised to direct to Figure 2 and Table 1
**Changes in text**: *demonstrated a reduction in observed rates (Table 1 and Figure 2)*

(7) Lines 206-207: "Salivary gland cancers demonstrated a statistically significant reduction for the Q1-4 period between 2019 and 2020."
Please cite Figure 2 and mark statistically significant results with asterisks in Figure 2. Besides, we suggest the authors describe all the statistically significant results, not just salivary gland cancers.

**Reply**: All statistically significant results have been discussed that are reported within the various subsites. Figure 2 has been cited to direct readers.
Changes in text: *Salivary gland cancers demonstrated a statistically significant reduction for the Q1-4 period between 2019 and 2020 as demonstrated in Figure 2*

(8) Lines 208-210: "When stratified by sex there is a consistent reduction in observed rates through the progression of quarters 1-4 in males yet in females there is a rise in rates in Q3 and 4 although the SIR is not statistically significant (Table 2)". Please make it clear that this is a comparison between 2020 and 2019.

**Reply**: We have added the years into the sentence to demonstrate difference between the 2 years.
**Changes in text**: reduction in observed rates from 2019 to 2020

(9) The data in Table 1 is consistent with the information presented in Figure 2, except for the data related to "Lip," which does not appear to be included in Figure 2.

**Reply**: Figure 2 has been revised to include Lip data
**Changes in text**: Please see revised Figure 2

(10) It seems that there is a discrepancy in the numbers in the "Expected" column for females in Table 2. The total should indeed add up to 122, not 123.

**Reply**: Thank-you for detecting this it has been corrected in Table 2
**Changes in text**: Please see revised Table 2

(11) We hope the authors consider using a flow diagram to state the numbers of individuals in the screening and analysis stages of this study. Besides, give reasons for non-participation at each stage. You could refer to our sister journal https://qims.amegroups.org/article/view/91253/html (Figure 1).

**Reply:** Thank-you for the suggestion the data we have is difficult to place into the suggested flow diagram. Due to the data being registry data and therefore doesn't have the same patient selection process and therefore the flow diagram may not be sufficient.

6. Discussion:
(1) Limitations should also include the possibility of misclassification of diseases in the database.

**Reply:** Tumors are coded by professional medical coders, many whom have years of experience. Misclassification is always possible, but we believe it would be rare in our dataset, especially since H&N cancers often have both hospital and pathology notifications.
**Changes in text:** *Disease misclassification within a large dataset is possible, within this database the risk is minimised by utilisation of medical coders classifying incoming data which is often cross referenced between both hospital and pathological notifications.*

(2) Differences in gender over time were not analyzed in the discussion. Each result should be analyzed and discussed.

**Reply**: Gender differences has been added to discussion with associated reference
**Changes in text**: We have added paragraph *Stratification of the oral cavity data demonstrated differences between gender and rates over the 2019-2020 period (Table 2). There was an increase in observed rates between 2019-2020 in females yet this was not statistically significant (SIR = 114.4 [95%CI 96.9-135.0], whilst males had a reduction which was for Q1-4 statistically significant (SIR = 83.7 [95%CI 73.7 – 95.0]). The differences in rates in oral cavity cancer and gender maybe explained by the rising incidence of oral cavity cancers in females, which has been reported in a multi institutional study by Clark et al in 2020. (20)*

# Minor concerns:
7. Please kindly identify the study design (cross-sectional, case-control, cohort study) in the Title or the Abstract.

**Reply**: Has been added into abstract cohort study
Changes in text:

8. Discussion: Future directions: You could also add that in nasopharyngoscopy, endoscopy, and other examinations, aerosol transmission may be caused, which may reduce these operational screening diagnostic methods. Therefore, it is necessary to strengthen and improve the protective measures in these procedures, as well as people's awareness (just for your reference).

Reply:
Changes in text:

9. Line 245-247: "The literature indicates that the COVID-19 pandemic has led to a reduction in cancer detection rates due to decreased utilization of cancer screening services, disrupted healthcare systems, patient reluctance to seek medical attention, and diversion of resources to COVID-19 management." Please cite references to back up these statements.

**Reply**: Citation has been added
**Changes in text**: 21. Alkatout, I., Biebl, M., Momenimovahed, Z et al (2021). Has COVID-19 Affected Cancer Screening Programs? A Systematic Review. Frontiers in oncology, 11, 675038.

10. Figures and Tables: Please cite the tables in order in the text. In addition, Figure 1 and Figure 2 were not mentioned in the text.

**Reply**: addition of citation for Figures
**Changes in text**: Figure 1 and 2 are both cited in the results section