**Title**

Impact of the COVID-19 pandemic on Stage and Incidence of Head and Neck Cancer: A Rapid Review and Meta-Analysis

**Abstract**

Objectives: This rapid review aims to evaluate the impact of the COVID-19 pandemic on incidence of head and neck cancer (HNC) and stage distribution at diagnosis.

Design: Rapid Review and Meta-analysis

Participants: comparative data for new HNC patients between a pre-pandemic cohort (before March 2020) and a pandemic cohort (after March 2020 during the lockdown period).

Main Outcomes Measured: data on tumour stage, incidence, referral pathway (number of new patient referrals) or workload levels (number of HNC treatments). Data on stage were summarised as odds ratios (OR) with 95% confidence intervals (CI), data related to changes in numbers of diagnoses, referrals and workload levels were summarised as a narrative synthesis.

Results: 31 reports were included in this review. Individually 16 out of 23 studies did not show a significant impact on stage relative to the pre-pandemic period. However, the meta-analysis revealed that patients diagnosed with HNC during the pandemic were 16% more likely to have nodal involvement (OR=1.16; 95% CI 1.00–1.35), 17% more likely to have a late overall stage (OR=1.17; 95% CI 1.01–1.36), and 32% more likely to present with advanced tumour extent (T3 and T4 stage) (OR=1.32; 95% CI 1.08–1.62). Data on incidence was extremely limited and not currently sufficient to assess trends in burden of disease.

Conclusions: This review indicates that during the COVID-19 pandemic there was upstaging of HNC at diagnosis, suggesting the provision of care to HNC patients was significantly affected.

**Key Points**

* The public health emergency caused by the coronavirus pandemic created major disruption to healthcare systems
* The public health message was to not use healthcare systems, it is unknown how this has impacted on head and neck cancer
* There is a lack of evidence as to the impact of the pandemic on head and neck cancer stage presentation, symptom duration and treatment intent.
* This rapid review demonstrated an upstaging of Head and Neck cancer at diagnosis suggesting provision of care was significantly affected by the COVID 19 pandemic
* It is still unclear if this stage shift will impact on mortality.

**Key Words**

COVID-19, COVID-19 pandemic, Head and neck cancer

**Introduction**

Worldwide, head and neck cancer (HNC) is responsible for approximately 900 000 cases and 400 000 deaths annually.1 In Europe and USA this represents 3-4% of annual cancer incidence.2,3 Early diagnosis and treatment are associated with reduced morbidity and mortality,4 with stage 1 disease having a 5-year survival rate of 80%, this falls to 30% for stage 4 disease.5

During the COVID-19 pandemic the frequency of primary care General Dental Practitioners (GDPs) and General Practitioners (GPs) consultations significantly reduced.6 This is a problem as primary care is responsible for approximately 90% of specialist referrals for HNC.7,8 Healthcare services around the world were put on an emergency footing with the cancellation of elective and non-emergency work to reallocate healthcare resources towards treating patients with COVID-19. Patient related anxieties,9 combined with public health messaging urging the population not to attend the health services unless absolutely necessary,10 also led to an avoidance in seeking medical care. This led to concerns that during the COVID-19 pandemic patients may have delayed presentation with HNC, resulting in reduced numbers of diagnoses or a stage shift that may result in excess morbidity and mortality.

This rapid review aims to quantify the impact of the COVID-19 pandemic on stage distribution at diagnosis and incidence of HNC. This will inform further recovery of services and highlight the gaps in the current evidence to guide further research in this area.

**Methods**

A pre-specified protocol was developed based on established PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) systematic review guidelines11 and The Cochrane Collaboration’s provisional rapid review method recommendations.12 The PICO (population, intervention, comparison and outcome) model for this review was:

* Population: Adult patients diagnosed with head and neck cancer (International Classification of Disease for Oncology, 3rd edition (ICD-O-3) diagnostic codes C00–C14, C30–32) during the COVID-19 pandemic.
* Intervention: COVID-19 pandemic (and associated public health measures).
* Comparison: Adult patients diagnosed with head and neck cancer before the COVID-19 pandemic (and associated public health measures).
* Outcomes: The stage at diagnosis, incidence of head and neck cancer diagnoses, volume of new patient referrals and volume of workload relating to treatments for HNC.

Eligibility criteria

Articles were eligible for inclusion if they provided: comparative data between a pre-pandemic (before March 2020) and pandemic cohort (after March 2020 during the lockdown period); provided comparative data on tumour stage, incidence, referral pathway (number of new patient referrals), or workload levels (number of treatments for HNC); reported effect on HNC.

Articles were excluded if they were: case reports, narrative review articles, news items, editorials, comments, letters, or conference abstracts; not published in English language; studies reported outcomes which were not related to tumour stage, incidence, referral pathway or workload levels; cohort comprised less than 15 subjects; studies investigating cancer in parts of the body other than head and neck; and studies that did not provide comparisons between pre-pandemic and pandemic cohorts.

Information sources

An extensive literature search was conducted using the following academic databases: PubMed, Scopus, Web of Science, and the China National Knowledge Infrastructure database. All publications between March 2020 and May 2022 were searched.

A grey literature search was also conducted using “grey matters”, a checklist developed by the Canadian Drug and Health Technology Agency (CDHTA) as a guide for the websites to search for health-related grey literature.13 Searches of MedRxiv (a pre-print server) and Google, were also made using the search terms listed below. The titles of the first 100 results for each grey literature website search were screened for relevance and the reports that met the parameters of the eligibility criteria were included in this review.

Search

Search terms “COVID”, “COVID-19”, “SARS-COV-2”, “coronavirus”, “pandemic” and “head and neck cancer” were combined with Boolean operators “AND” and “OR” to search the published reports in the databases and grey literature sources: “(COVID OR COVID-19 OR SARS-COV-2 OR coronavirus OR pandemic) AND (head and neck cancer)”. The database search was carried out on 9th May 2022.

Study Selection and Data Extraction

Duplicate studies were identified and removed using automated tools and manual searching. Two independent reviewers screened titles and abstracts of each article and exclude those that did not meet the parameters of the eligibility criteria. Of the remaining studies, the full text articles were then screened to assess whether they met the parameters of the eligibility criteria by two independent reviewers. Any disagreement on inclusion and classification between the reviewers at both screening stages was put to a third tie-breaker reviewer to resolve these conflicts. The remaining eligible studies were included in this review.

Primary data items that were collected from the eligible studies included: time interval of pre-pandemic and pandemic cohorts; TNM classification of Malignant tumours 8th edition and AJCC (American Joint committee on cancer) or UICC (Union for international cancer control) overall staging classification of head and neck tumours14,15; total number of patients; incidence, referrals, or workload levels; relevant conclusions. Secondary data items that were collected included: country study was conducted and patient demographics including age and sex.

Methodological Quality Assessment

Newcastle-Ottawa quality assessment scale was used to assess included studies for patient selection (maximum 4 stars), comparability between subjects (maximum 2 stars) and assessment of outcome (maximum 3 stars), although due to the retrospective nature of the studies included, adequacy of follow up could not be assessed. Each study was given a score out of 9 based on this scale.

Statistical Analysis

The data was analysed using Review Manager (RevMan) V5.4.1 (The Cochrane Collaboration, 2020). Odds Ratios (OR), 95% confidence Intervals (95%CI) and relevant P-values were calculated for the pooled analysis of each dichotomous outcome using a random effects model. Heterogeneity between included studies was expected due to regional and institutional variation in COVID-19 related service disruption, COVID-19 prevalence and geography. Statistical heterogeneity was calculated using Higgin’s I2 statistic with a relevant P-value. P-values of less than 0.05 were considered significant. Forrest plots were produced for each outcome.

Leave-one-out sensitivity analysis was performed on outcomes with statistically significant Higgin’s I2 test for heterogenicity or with statistically significant effect sizes. One study was removed at a time from the model and the effect was observed to identify if any study was an outlier responsible for high heterogenicity or the large effect size.

**Results**

**Literature Search and Study Selection**

The initial searches identified 894 published articles across the four academic databases containing potentially relevant information. An automated duplicate search followed by a manual duplicate search of the results identified 279 duplicate articles, which were removed before the screening process. The title and abstracts of the remaining 615 articles were thoroughly screened, to exclude articles that although contained search terms, but did not meet the parameters of the eligibility criteria. 46 full text articles that contained potentially relevant information were sought for retrieval, but three were not able to be retrieved. 13 full text articles were excluded after full text review, the reasons for exclusion were recorded and summarised (Figure 1), resulting in 30 published articles being included in this review.

There were 61 websites investigated as part of the grey literature search strategy, mainly health-related government agencies around the world, but also a pre-print server and online search engine. This resulted in one relevant report (Grey literature, Figure 1) being identified and included in this review. The full literature search process is summarised on the PRISMA flow chart (Figure 1).

**Study Characteristics**

Table 1 lists the study characteristics of each of the included studies with information on time intervals for data collection, cohort characteristics, and quality assessment rating. This review included 23 studies investigating the effect on cancer stage, with nine of these studies also reporting an effect on the number of HNC diagnoses. This review also included seven studies investigating the effect on diagnoses, referrals or workload levels of HNC and one government report investigating the effect on HNC incidence. The included studies were conducted in 13 different countries across North America, Europe, Australia, and Asia. Total sample sizes ranged from 44 to 3333, with many studies reporting data from small samples collected at a single institution. There was also considerable variation in the time intervals for data collection between the studies, which varied from 1 month up to 12 months.

There were 20 studies eligible for inclusion in the meta-analysis, however, due to differences in reporting of cancer stage, not all the studies could be analysed together. Of the included studies, 13 measured stage using TNM and were included in the meta-analysis of TNM stage. But stage was reported differently between them; six studies reported the data for tumour extent (T), lymph nodes (N) and metastasis (M) stage, six studies reported only the tumour and node stages and one study reported only the effect on tumour stage. There were 16 studies which reported the effect on AJCC/UICC clinical stage, all of which were included in the meta-analysis. Eight of these also provided TNM data for each cohort so were included in both analyses. The remaining three studies investigating stage were excluded from the meta-analysis as they did not provide enough stage or cohort data to be compatible for statistical evaluation.

**Descriptive Results**

**Effect on Stage of Head and Neck cancer**

The effect of the COVID-19 pandemic on HNC stage was investigated by 23 observational studies. Individually, 16 of the 23 studies investigating stage did not report a significant shift in stage between pre-pandemic and pandemic cohorts.16-31 However, many of these studies did report upshifts in tumour stage27,28, metastasis stage29, or overall clinical stage30,31 but the magnitude of the effect was not large enough individually to reach the threshold of statistical significance.

These conclusions seem to contradict the findings of the meta-analysis indicating a statistically significant increase in stage. The meta-analysis showed for AJCC/UICC stage, late stage was most commonly encountered in both pre-pandemic (54%) and pandemic (57%) cohorts (Table 2). There was a significantly higher proportion of late-stage cases during the pandemic (Figure 2a), and significantly fewer early cases compared with pre-pandemic time periods (Figure 2b). In studies that reported TNM stage there were no statistically significant differences in the proportion of patients presenting with metastasis involvement (Figure 3), but significantly more tumours presented at T3 and T4 stage (p=0.007) (Figure 4a), more with lymph node involvement (p=0.04) (Figure 5) and fewer at T1 and T2 stage (p=0.01) (Figure 4b) during the pandemic.

The sensitivity analysis found that the study by Balk et al29 was responsible for most of the heterogeneity observed in the M1 stage outcome. After removing the study the OR increased in magnitude (1.18 [0.61-2.27] P=0.62) but the overall effect remained not statistically significant. Tevetoğlu et al32 was responsible for the heterogeneity observed in T1 and T2, as well as the T3 and T4 outcome, after removing the study this reduced the magnitude of the observed effect, but the effect remained statistically significant.

**Effect on Incidence of Head and Neck cancer**

The effect of the COVID-19 pandemic on incidence was measured by one government report from Public Health Scotland. This analysis of cancer registry data found a 3% fall in annual incidence of HNC in 2020 compared with the previous year (n = 1265 vs 1228,) however, this reduction was in line with long-term trends and within the expected range of values predicted for 2020.33

There were 16 observational studies also included in this review that investigated a range of predictors of changes in disease burden - the number of diagnoses, number of referrals, or workload levels. Two studies that were conducted in Germany reported there were no trends toward lower incidence during the pandemic.28,29 Seven studies investigating the effect on the number of diagnoses23,24,26,31,34-36 had a mean reduction of 29.8% (range 14% to 59.5%) during the pandemic, compared with pre-pandemic periods. Referrals followed a similar trend with a mean reduction of 56.85% (range 35% to 75%) across four studies.25,37-39 Three additional studies investigating workload changes within hospital departments with reductions in the numbers of HNC treatments of between 8.91% and 55%.40-42

**Newcastle-Ottawa Quality Assessment**

We analysed the methodological quality of the included studies using the Newcastle-Ottawa quality assessment scale. Studies scored poorly for comparability between cohorts, as most did control for sample differences in baseline characteristics, so were prone to confounder biases. Four studies had a NOS score between 7–9 and were deemed to have high methodological quality, 27 studies had a NOS score between 4–6 and were deemed to have mediocre methodological quality. The mean NOS score of the studies included in this review was 5.

**Discussion**

Worldwide, many health services had to stop or reduce their activities during the COVID-19 pandemic, as healthcare resources were prioritised to maintain sufficient capacity to treat COVID-19 patients, leading to a decrease in routine elective and non-covid emergency work.43,44 It is therefore hypothesised that the unprecedented pressures, could compound to potentially delay patient presentation resulting in upshifting of disease stage. Models have predicted that these large alterations to clinical practice would lead to disease stage upshifting of missed HNC cases, increasing morbidity and mortality.45,46

This meta-analysis provides evidence of the impact of the COVID-19 pandemic has had on HNC stage globally. Patients diagnosed with HNC during the pandemic were 16% more likely to have nodal involvement, 17% more likely to have a late overall stage, and 32% more likely to present with an advanced tumour extent of stage T3 or T4. This is a concerning finding as stage is closely linked to morbidity and mortality.5 These results show that there was a profound effect of lockdown restrictions during the period following March 2020, but it does not indicate the effect on the following periods when restrictions were eased, and primary care services began to recover and resume delivery of care to non-covid and non-emergency patients. By not accounting for the longer-term trends in HNC, it is difficult to be certain whether this is an artefact of fewer patients coming forward during the first few months of lockdown or a more concerning long-term global trend in which there is a backlog of undiagnosed HNC cases causing disease to upshift over many years. Future studies should focus on investigating this post-pandemic period to measure the potential long-term implications from the pandemic.

Currently, the available literature is inconclusive on the effect of the COVID-19 pandemic on the incidence of HNC. This review found most studies had small sample sizes comprising less than 100 subjects, so a small difference in numbers led to a large percentage difference making it difficult to draw firm conclusions about the magnitude of any change in disease burden during the lockdown. Another source of inaccuracy comes from comparing two groups without considering long-term trends in the numbers of HNC cases, assuming that numbers will remain this same year on year. However, this is not the case as incidence of HNC fluctuates,47 and it is difficult to know how much of the change reported by these studies are due to normal fluctuations and how much are caused by the pandemic. Consequently, future studies should focus on analysing population level cancer registry data and adjusting for long-term trends.

Many studies were analysing data from an institution or regional level, which introduces a selection bias as the results as one institution/region may not accurately reflect the picture at a national level. An example of this effect can be observed in the results of Flynn et al which reported 11% more patients in the 2020 cohort compared to 2019 cohort in the West of Scotland between the time intervals sampled.48 However, at a national level, in Scotland, there was a 3% reduction in HNC cases in 2020 compared with 2019.33 This indicates the potential inaccuracies of extrapolating trends that may be observed in small studies to a national level.

Small sample sizes resulted in many studies being underpowered individually to detect a significant stage shift. Despite 70% of the studies reporting stage finding no significant difference in stage between the pre-pandemic and pandemic cohorts, when the data were combined in a meta-analysis there was a statistically significant upshifting in cancer stage. Future studies should focus on having large sample sizes which are suitably powered to detect significant changes in stage.

There is usually a three-year delay in the reporting of most cancer registry data. This lag is mainly to ensure data completeness in the ascertainment of cancer cases and the coming to light of death certification, which is necessary to accurately report incidence and mortality of cancer.49 As a result most of the government agencies responsible for publishing population-level reports about cancer did not provide analysis of data beyond the year 2019. This was likely the reason the grey literature search, which included many government agencies, did not identify many relevant reports on this topic and is the reason most studies investigating the effect of lockdown measures on HNC use data from an institutional level.

One limitation of this review is that the evaluated outcomes were inconsistently measured and reported across the included studies, with different stage classifications, different types of referrals and different activities measured for workload levels. As mentioned earlier, the majority of included studies did not control for differences in baseline characteristics between the cohorts presenting a confounding bias and were analysing data from a single institution introducing a selection bias. This was also a review of retrospective studies with data reliant upon the accuracy of previous documentation and observational data which cannot prove causation. Compared with a systematic review, this rapid review methodology was more limited in scope as it only searched four databases and had a more restrictive inclusion criteria.

**Conclusion**

This rapid review found that during the COVID-19 pandemic there was an initial upshifting of HNC stage suggesting the provision of care to HNC patents was significantly affected, but it is unclear whether this stage shift reflects a transient or long-lasting change and whether it will impact on long-term survival outcomes. The review also found there were limited data on HNC incidence during the pandemic yet available to fully assess trends in the burden of disease.

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52 Lucidi, D. *et al.* Head and Neck Cancer During Covid-19 Pandemic: Was there a Diagnostic Delay? *Indian Journal of Otolaryngology and Head and Neck Surgery*, doi:10.1007/s12070-021-03050-5 (2022).

53 Riju, J. *et al.* Analysis of Early Impact of COVID-19 on Presentation and Management of Oral Cancers - an Experience from a Tertiary Care Hospital in South India. *Indian Journal of Surgical Oncology* **12**, 242-249, doi:10.1007/s13193-021-01302-y (2021).

***Figure 1*** *PRISMA flowchart of Study Selection*

**Identification of studies via databases and grey literature**

Records identified from:

Databases (n = 894)

Records removed *before screening*:

Duplicate records removed (n = 279)

Records marked as ineligible by automation tools (n = 0)

Records removed for other reasons (n = 0)

Title/abstracts screened

(n = 615)

Excluded

(n = 569)

Reports sought for retrieval

(n = 46)

Reports not retrievable

(n = 3)

Reports assessed for eligibility

(n = 43)

Reports excluded:

Publication type (n = 7)

Contained <15 subjects (n = 1)

Did not report effect on stage, incidence or referral (n = 4)

Did not investigate HNC (n = 1)

Reports included in review

(n = 31)

Studies included in meta-analysis (n = 20)

**Identification**

**Screening**

**Included**

Grey Literature

(n = 1)

***Table 1*** *Included Study Characteristics*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  |  |  | **Pre-pandemic vs Pandemic Cohort n** | | |  |
| **Study** | **Country** | **Time Intervals Sampled** | **Total Patients** | **Mean age (±SD or range)** | **Sex (male/Female)** | **Newcastle-Ottawa Quality Assessment Scale** |
| Murri et al 202116 | Italy | March 2019 – December 2019 March 2020 – December 2020 | 25 vs 19 | 69.24 ±0.94 vs 69.31 ±14.43 | 24/1 vs 15/4 | 5 |
| Stevens at al 202250 | USA | March 2019 – July 2019 March 2020 – July 2020 | 134 vs 134 | 62.9 ±11.9 vs 64.5 ±10.5 | 101/33 vs 98/36 | 8 |
| Akbari et al 2022 51 | Iran | April 2019 – April 2020 April 2020 – April 2021 | 102 vs 116 | 59 ±9.51 vs 59.59 ±9.27 | 90/12 vs 111/5 | 4 |
| Flynn et al 202248 | UK | June 2019 – October 2019 June 2020 – October 2020 | 250 vs 278 | 65 (26–96) vs 65 (23–100) | 185/65 vs 185/93 | 8 |
| Popovic et al 202217 | Italy | September 2019 – February 2020 March 2020 – May 2020 | 53 vs 17 | 69.6 ±14.8 vs 70.0 ±10.3 | N/A | 8 |
| Venkatasai et al 202218 | India | October 2019 – February 2020 March 2020 – July 2020 | 51 vs 25 | 55 (19–78) vs 50 (35–71) | 40/11 vs 21/4 | 4 |
| Lucidi et al 202252 | Italy | March 2019 – October 2019 March 2020 – October 2020 | 140 vs 125 | 68.5 ±12.2 vs 66.4 ±13.3 | N/A | 6 |
| Riju et al 202153 | India | April 2019 – March 2020 April 2020 – June 2020 | 192 vs 26 | 51.08 ±12.18 vs 51.27 ±12.86 | 142/50 vs 17/9 | 5 |
| Szewczyk et al 202119 | Poland | February 2019 – February 2020 March 2020 – February 2021 | 278 vs 340 | 63.6 vs 64.1 | 206/72 vs 263/77 | 6 |
| Tan et al 202127 | Australia | August 2019 – March 2020 March 2020 – October 2020 | 64 vs 63 | 65.7 (26.2–95) vs 67.1 (45.3–92.7) | 17/47 vs 22/41 | 5 |
| Tevetoğlu et al 202132 | Turkey | March 2019 – September 2019 March 2020 – September 2020 | 60 vs 56 | 60.3 ±8.6 vs 64.2 ±10.01 | 49/11 vs 48/8 | 4 |
| Thompson et al 202220 | USA | March 2019 – May 2019 March 2020 – May 2020 | 69 vs 117 | 65.2 vs 63.5 | 51/18 vs 77/40 | 4 |
| Wai et al 202130 | USA | March 2019 – April 2019 March 2020 – April 2020 | 83 vs 56 | 58 ±15 vs 53 ±15 | 51/32 vs 34/22 | 4 |
| Yao et al 202121 | USA | September 2019 – January 2020 March 2020 – July 2020 | 68 vs 26 | 55 (47–72)\*\* vs 70 (65–82)\*\* | 34/34 vs 17/9 | 6 |
| Bhamra et al 202239 | UK | February 2019 – April 2019 February 2020 – April 2020 | 38 vs 31 | N/A | N/A | 4 |
| Heimes et al 202128 | Germany | March 2019/18 – June 2019/18\* March 2020 – June 2020 | N/A | N/A | N/A | 6 |
| Schoonbeek et al 202236 | Netherlands | June 2019 – December 2019 June 2020 – December 2020 | 1635 vs 1698 | 66.1 ±12.0 vs 66.4 ±12.4 | 1098/537 vs 1114/584 | 6 |
| Solis et al 202123 | USA | September 2019 – March 2020 March 2020 – September 2020 | 77 vs 60 | 65 (43–92) vs 67 (23–87) | 53/25 vs 46/14 | 6 |
| Kiong et al 202124 | USA | May 2019 – June 2019 May 2020– June 2020 | 128 vs 103 | 64 (22–95) vs 65 (27–89) | 121/35 vs 87/30 | 6 |
| Drake et al 202225 | UK | March 2019 – May 2019 March 2020 – May 2020 | 118 vs 118 | 63.7 ±10.8 vs 61.5 ±10.0 | 80/38 vs 91/27 | 5 |
| Balk et al 202229 | Germany | March 2019 – March 2020 April 2020 – April 2021 | 319 vs 293 | 63.27 ±11.89 vs 62.48 ±11.87 | 236/83 vs 216/77 | 6 |
| Ruiz-Medina et al 202126 | Spain | March 2019 – March 2020 March 2020 – March 2021 | 108 vs 92 | N/A | N/A | 6 |
| Gazzini et al 202131 | Italy | May 2019 – March 2020 March 2020 – January 2021 | 79 vs 45 | 70.3 vs 69.4 | N/A | 6 |
| Ralli et al 202140 | Italy | March 2019 – March 2020 March 2020 – March 2021 | 101 vs 92 | N/A | N/A | 5 |
| De Luca et al 202234 | Italy | March 2015–19 – November 2015–19\* March 2020 – November 2020 | N/A | N/A | N/A | 5 |
| Taylor et al 202037 | UK | January 2020 April 2020 | N/A | N/A | N/A | 4 |
| Peacock et al 202135 | Belgium | January 2019 – December 2019 January 2020 – December 2020 | N/A | N/A | N/A | 6 |
| Abelardo at al 202238 | UK | April 2019 – November 2019 April 2020 – November 2020 | 862 vs 557 | 65 (3–96) vs 63 (6–99) | 375/487 vs 263/294 | 5 |
| Belmont et al 202041 | France | December 2019 – February 2019 March 2020 – May 2020 | N/A | N/A | N/A | 5 |
| Morrison et al 202042 | USA | March 2019 – April 2019 March 2020 – April 2020 | N/A | N/A | N/A | 4 |

N/a – data not provided

\*average of preceding years

\*\*(IQR)

***Table 2*** *Pooled Meta-Analysis Outcomes*

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Outcome** | **Number of Studies** | **Total Number of Patients** | **Patients in Pre-Pandemic Cohort**  **n (%)** | **Patients in Pandemic Cohort**  **n (%)** | **OR** | **95% CI** | **Overall Effect P-Value** | **I2** | **I2 p-value** |
| **TNM Stage** | | | | | | | | | |
| T1 and T2 | 13 | 3288 | 1005 (57) | 791 (51) | 0.76 | 0.62–0.94 | 0.010 | 43% | 0.05 |
| T3 and T4 | 13 | 3288 | 752 (43) | 739 (49) | 1.32 | 1.08–1.62 | 0.007 | 42% | 0.06 |
| N1 or > | 12 | 3133 | 752 (45) | 732 (50) | 1.16 | 1.00–1.35 | 0.04 | 0% | 0.62 |
| M1 | 6 | 1862 | 49 (5) | 31 (4) | 0.87 | 0.41–1.86 | 0.72 | 46% | 0.10 |
| **Overall AJCC/UICC Stage** | | | | | | | | | |
| Early Stage (I or II) | 16 | 7020 | 1620 (44) | 1389 (41) | 0.85 | 0.73–0.98 | 0.02 | 26% | 0.16 |
| Late Stage (III or IV) | 16 | 7020 | 1979 (54) | 1933 (57) | 1.17 | 1.01–1.36 | 0.03 | 28% | 0.14 |

***Figure 2a*** *Overall AJCC/UICC Late-Stage Forest Plot*

*Table

Description automatically generated*

***Figure 2b*** *Overall AJCC/UICC Early-Stage Forrest Plot*

Table

Description automatically generated

***Figure 3*** *M1 Stage Forest Plot*

*Table

Description automatically generated with medium confidence*

***Figure 4a*** *T3 and T4 Stage Forest Plot*

***Table

Description automatically generated***

***Figure 4b*** *T1 and T2 Stage Forest Plot*

*Table

Description automatically generated*

***Figure 5*** *N1 or > Stage Forest Plot*

*Table

Description automatically generated*

***Table 3*** *Newcastle-Ottawa Quality Assessment Scale Scores of Included Studies*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Study** | **Selection (MAX 4)** | **Comparability (MAX 2)** | **Outcome (MAX 3)** | **Total (MAX 9)** |
| Murri et al 2021 | \*\*\* |  | \*\* | 5 |
| Stevens at al 2022 | \*\*\*\* | \*\* | \*\* | 8 |
| Akbari et al 2022 | \*\* |  | \*\* | 4 |
| Flynn et al 2022 | \*\*\*\* | \*\* | \*\* | 8 |
| Popovic et al 2022 | \*\*\*\* | \*\* | \*\* | 8 |
| Venkatasai et al 2022 | \*\* |  | \*\* | 4 |
| Lucidi et al 2022 | \*\*\*\* |  | \*\* | 6 |
| Riju et al 2021 | \*\*\* |  | \*\* | 5 |
| Szewczyk et al 2021 | \*\*\*\* |  | \*\* | 6 |
| Tan et al 2021 | \*\*\* |  | \*\* | 5 |
| Tevetoğlu et al 2021 | \*\* |  | \*\* | 4 |
| Thompson et al 2022 | \*\* |  | \*\* | 4 |
| Wai et al 2021 | \*\* |  | \*\* | 4 |
| Yao et al 2021 | \*\*\*\* |  | \*\* | 6 |
| Bhamra et al 2022 | \*\* |  | \*\* | 4 |
| Heimes et al 2021 | \*\*\*\* |  | \*\* | 6 |
| Schoonbeek et al 2022 | \*\*\*\* |  | \*\* | 6 |
| Solis et al 2021 | \*\*\*\* |  | \*\* | 6 |
| Kiong et al 2021 | \*\*\*\* |  | \*\* | 6 |
| Drake et al 2022 | \*\*\* |  | \*\* | 5 |
| Balk et al 2022 | \*\*\*\* |  | \*\* | 6 |
| Ruiz-Medina et al 2021 | \*\*\*\* |  | \*\* | 6 |
| Gazzini et al 2021 | \*\*\*\* |  | \*\* | 6 |
| Ralli et al 2021 | \*\*\* |  | \*\* | 5 |
| De Luca et al 2022 | \*\*\* |  | \*\* | 5 |
| Taylor et al 2020 | \*\* |  | \*\* | 4 |
| Peacock et al 2021 | \*\*\*\* |  | \*\* | 6 |
| Abelardo at al 2022 | \*\*\* |  | \*\* | 5 |
| Belmont et al 2020 | \*\*\* |  | \*\* | 5 |
| Morrison et al 2020 | \*\* |  | \*\* | 4 |