Fewer head and neck cancer diagnoses and faster treatment initiation during COVID-19 in 2020: A nationwide population-based analysis

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Original Article

Fewer head and neck cancer diagnoses and faster treatment initiation during COVID-19 in 2020: A nationwide population-based analysis

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ABSTRACT

Background: Inevitably, the emergence of COVID-19 has impacted non-COVID care. Because timely diagnosis and treatment are essential, especially for patients with head and neck cancer (HNC) with fast-growing tumours in a functionally and aesthetically important area, we wished to quantify the impact of the COVID-19 pandemic on HNC care in the Netherlands.

Material and Methods: This population-based study covered all, in total 8468, newly diagnosed primary HNC cases in the Netherlands in 2018, 2019 and 2020. We compared incidence, patient and tumour characteristics, primary treatment characteristics, and time-to-treatment in the first COVID-19 year 2020 with corresponding periods in 2018 and 2019 (i.e. pre-COVID).

Results: The incidence of HNC was nearly 25% less during the first wave (n = 433) than in 2019 (n = 595) and 2018 (n = 598). In April and May 2020, the incidence of oral cavity and laryngeal carcinomas was significantly lower than in pre-COVID years. There were no shifts in tumour stage or alterations in initial treatment modalities.

Regardless of the first treatment modality and specific period, the median number of days between first visit to a HNC centre and start of treatment was significantly shorter during the COVID-19 year (26–28 days) than pre-COVID (31–32 days, $p < 0.001$).

Conclusion: The incidence of HNC during the Netherlands' first COVID-19 wave was significantly lower than expected. The expected increase in incidence during the remainder of 2020 was not observed. Despite the overloaded healthcare system, the standard treatment for HNC patients could be delivered within a shorter time interval.

The emergence of COVID-19, the novel coronavirus disease caused by SARS-CoV-2 and declared to be a pandemic in March 2020 by the World Health Organization [1], disrupted healthcare systems worldwide [2–6], and continues to do so.

Non-COVID care has been greatly affected by the diversion of health-care resources towards COVID-19 care and also by the restrictive measures introduced to contain further outbreaks [7,8]. For example, social distancing measures urging vulnerable and/or elderly people to stay at home as much as possible led some patients to delay taking action. Although medical help is indicated, patients with head and neck cancer (HNC) can be hesitant to seek it; most are elderly, and many are frail and socially isolated [9–11]. Due to their underlying illness, and often to their immunosuppressed status, these patients' vulnerability to severe COVID-19-related complications added to the impact of the pandemic on them [2].

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Furthermore, allied healthcare delivery such as dental care is – especially in those with oral cavity carcinomas – essential for timely recognition and referral. However, this was also restricted during the first outbreak [12]. General practitioners (GPs) were also overloaded and there were widespread perceptions that medical resources were being diverted solely to COVID care. Many patients also assumed that a visit to their GP or a hospital would increase their risk of infection with SARS-CoV-2 [13]. As a result, the overall number of newly diagnosed cancer patients declined in the first COVID-19 period [14,15], and delays in diagnosis and treatment resulted from the limited availability of resources and the diversion of healthcare capacity towards COVID-19 care. As HNC tends to grow rapidly in functionally and aesthetically important regions, timely diagnostic workups and short time-to-treatment intervals are essential [16–18]. Delays in detection in this population can negatively affect not only tumour stage and the intent and intensity of treatment [4,15,19–21], but also oncological and functional outcomes and patients' subsequent quality of life [17,18].

HNC care in the Netherlands is centralized at eight head and neck oncology centres (HNOCs) and their six preferred partner hospitals. As almost all these specialized hospitals were also key healthcare providers for COVID-19 patients, the best way of allocating the limited resources between COVID-19 and cancer patients was sometimes a difficult dilemma [22,23].

With a view to possible future crises and circumstances with limited resources, and to help define the lessons learned, we wished to quantify the impact of the pandemic on HNC diagnosis and care in the Netherlands. We therefore compared the incidence of HNC, distribution of subsites and tumour stages, time-to-treatment intervals and administered primary treatment modalities between the first COVID-19 pandemic year, including the first wave and the recovery period, and corresponding periods in 2018 and 2019.

Material and methods

Patients

To assess the incidence of HNC, we used the Netherland Cancer Registry (NCR) to select all patients with a pathologically confirmed first primary head and neck malignancy who presented in 2018, 2019 or 2020. This selection included squamous cell carcinoma of pharynx, larynx, or oral cavity as well as salivary gland cancers, nasal cavity carcinoma and cervical lymph node metastasis of squamous cell cancer of an unknown primary tumour (CUP). We excluded those with in situ carcinomas, recurrent malignancy or any synchronous primary tumour in the head and neck region. We also excluded patients with cutaneous malignancies, sarcomas, neuroendocrine cancers or lymphomas in the head and the neck region, and also those with thyroid carcinomas.

We used patient characteristics (sex and age at diagnosis), tumour characteristics (subsite, clinical tumour stage), and primary treatment characteristics (treatment modality and date of first treatment), as well as the date of diagnosis and date of first consultation per hospital.

This retrospective observational study does not fall under the scope of the Medical Research Involving Human Subjects Act (WMO).

Definitions

We defined the first wave of the COVID-19 pandemic in the Netherlands as the period between 15 March and 1 June, i.e. the period of the first lockdown. This period was characterised by the nationwide closure of schools, restaurants, bars and sporting facilities, the implementation of social distancing policies, and the halting of nationwide screening programs for breast, colorectal and cervical cancer. The remaining months of 2020, starting from 1 June and ending 31 December, were expected to be recovery months following the first wave. Within this recovery period, the second lockdown was likewise defined based on social restrictions imposed by the government and started 14 October until 31 December.

The clinical stage of disease was defined according to the eighth edition of the Union for International Cancer Control TNM classification of malignant tumours (cTNM8).

Primary treatment was subdivided into surgery with or without adjuvant therapy; radiotherapy with or without concomitant systemic therapy; other therapies; and no primary treatment.

Two time intervals were assessed: (1.) the care pathway interval (CPI), i.e. the number of days from the first visit to an HNOC or preferred partner hospital to start of treatment in that hospital; and (2.) the time-to-treatment interval (TTI), i.e. the number of days between histopathological biopsy and the start of treatment [24]. Patients whose dates were unknown and those who did not receive primary treatment were not included in CPI or TTI analyses. Additionally, patients with a TTI of zero days were excluded from TTI analyses, since the diagnostic intervention for most of them turned out to be therapeutic (e.g. transoral laser excision of T1a glottic laryngeal carcinoma). Patients who started radiotherapy within seven days of an intravenous loading dose of cetuximab were included in the initial radiotherapy group, with the first date of radiotherapy as the start of treatment. The CPI and TTI were also categorized on the basis of the Dutch quality indicator, stating that 80% of patients with HNC should start treatment within 30 days of first visit to an HNOC. CPI and TTI were additionally assessed by first treatment modality: surgery, radiotherapy, or other.

Statistical analysis

The total number of patients with newly diagnosed HNC was counted in absolute numbers. We calculated crude rates (CR) per 1,000,000 per incidence month, for HNC total and by subsite and stage (low (I/II) or high (III/IV) stage). The incidence rate ratio was calculated to test differences between CRs between the years. Percentual changes per incidence month were calculated by comparing the observed monthly incidence with the expected monthly incidence based on averages of 2018 and 2019.

Chi-squared tests or Fisher's exact tests were used to establish any differences between the proportions of patients with certain tumour and treatment characteristics (subsite, stage, treatment modality, and CPI and TTI as dichotomized values) between periods (first COVID-19 wave and separately the following recovery period, both vs. corresponding pre-COVID periods in 2018 and 2019 combined). The Mann-Whitney U test was used to compare the continuous CPI and TTI. Data were analysed using STATA (StataCorp. 2017. *Stata Statistical Software: Release 16.1*. StataCorp LLC, College Station, TX).

Results

During the first five months of 2020 there was a fall in the incidence of newly diagnosed HNC cases in the Dutch population (CR, Fig. 1*A*); in April and May (i.e. the first wave), the incidence was significantly lower than in the same months in 2018 and 2019. The overall CR in April 2020 was 9.1 per 1,000,000 inhabitants, vs. 11.8 in April 2018 (p = 0.017) and 12.7 in April 2019 (p = 0.001) (*Supplementary Table 1)*. A similar and significant trend was seen in May 2020. In April 2020, 33% fewer patients were diagnosed with HNC compared to the expected mean monthly incidence based on preceding years (Fig. 1*B*). A significant increase in incidence during the remaining months of 2020 was not observed. Although an apparent second COVID-19 wave took place during

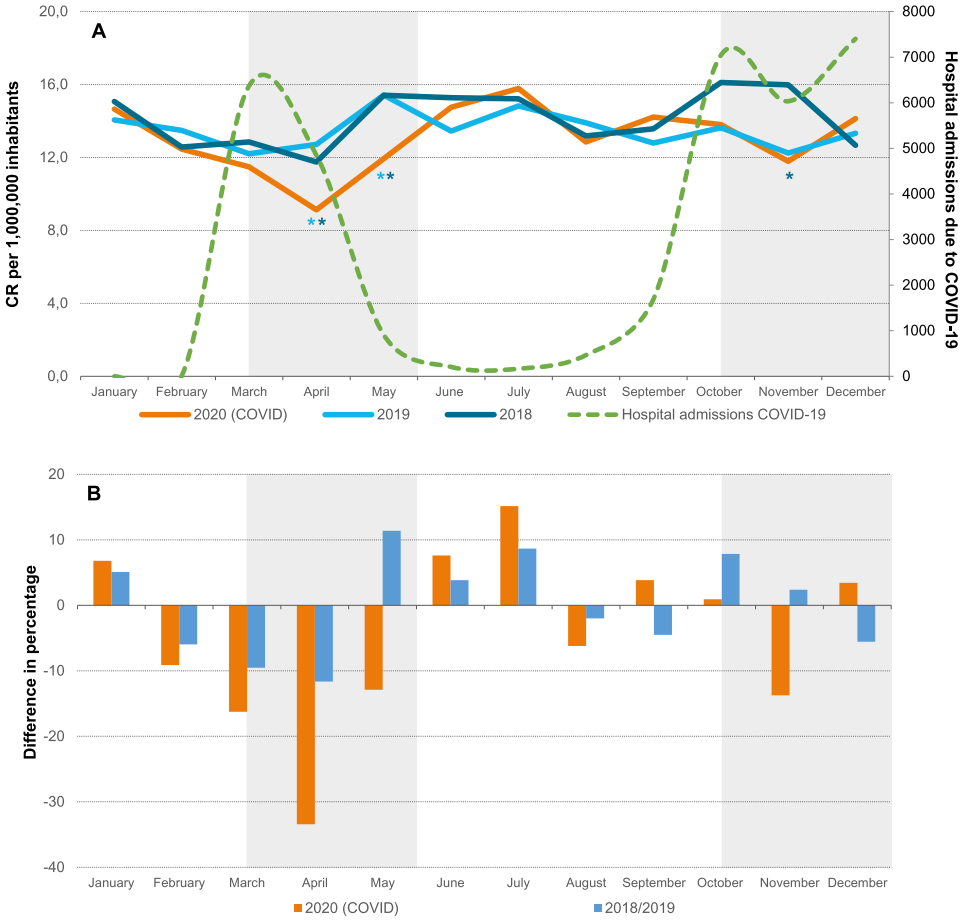

Fig. 1. A: Incidence (crude rate) for head and neck cancer in the Netherlands during COVID-19 (2020, orange) vs. pre-COVID (2018 and 2019, dark and light blue)[a]. B: Percentual difference of monthly incidence in 2020 (orange) and 2018/2019 (blue) compared to expected monthly incidence (n = 239) based on the monthly average in 2018/2019[a]. [a]The green dotted line shows the trend of COVID-19 related hospital admissions, marking the periods in which the healthcare system was overloaded, corresponding with the two following COVID-19 waves and accompanying lockdown measures. The grey background blocks indicate the Netherlands' first and second COVID-19 wave and the accompanying lockdown measures (15 March – 1 June 2020, 14 October – 31 December 2020, respectively). The asterisks indicate a significant difference for 2018 vs. 2020 (COVID, dark blue asterisk) and for 2019 vs. 2020 (COVID, light blue asterisk).

the fall of 2020, this did not result in yet another significant decline in incidence.

HNC incidence for the four major subsites are displayed in Fig. 2. In April and May 2020, the incidence of laryngeal carcinoma in particular was significantly less compared to preceding years (Fig. 2*D*). But while the incidence pattern of oral cavity carcinoma in May was similar (Fig. 2*A*), there was no apparent decline in patients presenting with an oropharyngeal or hypopharyngeal carcinoma (Fig. 2*B-C*). However, for these two subsites, a significant increase in incidence was reported in December 2020 (vs. 2018/2019). Apart from this month, a trend towards increased incidences was not observed.

Stratified analyses by stage *(Supplementary Fig. 1)* showed an equal pattern of stage I/II and stage III/IV incidence rates.

During the Netherlands' first COVID-19 wave (15 March – 1 June), a total of 433 patients were diagnosed with HNC (corresponding periods: 2019, n = 595; 2018, n = 598). Patient, tumour, and treatment characteristics during the first COVID wave were similar to those in the two preceding years (*Supplementary Table 2*).

Baseline characteristics of the patients presenting in the months following the first wave (1 June – 31 December 2020) show comparable absolute incidence, age, and sex (Table 1). The two tumour sites with the highest incidence were the oral cavity (27.3%) and larynx (23.1%), and the proportional distribution across subsites was not statistically different in the COVID year compared to preceding years. Relative to the two preceding years, a borderline significant stage shift was observed with an increase of stage IV tumours at the expense of stage I-III tumours (p = 0.093).

The distribution of treatment modalities during the pandemic year 2020 did not differ from that in 2018 and 2019.

During the first outbreak, both time-to-treatment intervals decreased significantly. The median CPI decreased from 31 days pre-COVID to 26 days during COVID (p < 0.001, Fig. 3). The proportion of patients starting treatment within 30 days increased significantly from 48.8% pre-COVID to 67.6% during COVID (p < 0.001, Table 2). The median TTI also decreased, from 37 days pre-COVID to 30 days during the first outbreak (p < 0.001, Fig. 3), whereas the number of excluded patients due to a TTI of zero days did not differ (n = 26 (7.1%) during COVID and n = 77 (7.6%) pre-COVID).

Throughout the recovery period in 2020, improvements persisted with slightly smaller significant differences (Fig. 3, Table 2). The proportion of patients with a TTI of 1–30 days also increased from 31.2% pre-COVID to 41.0% during COVID (p < 0.001). This proportion increased in all treatment types and was especially evident for surgically treated patients (from 34.4% pre-COVID to 44.2% during COVID, p < 0.001).

Discussion

Our results show that the incidence of HNC in the Netherlands was significantly lower during the first COVID-19 wave in 2020 (a

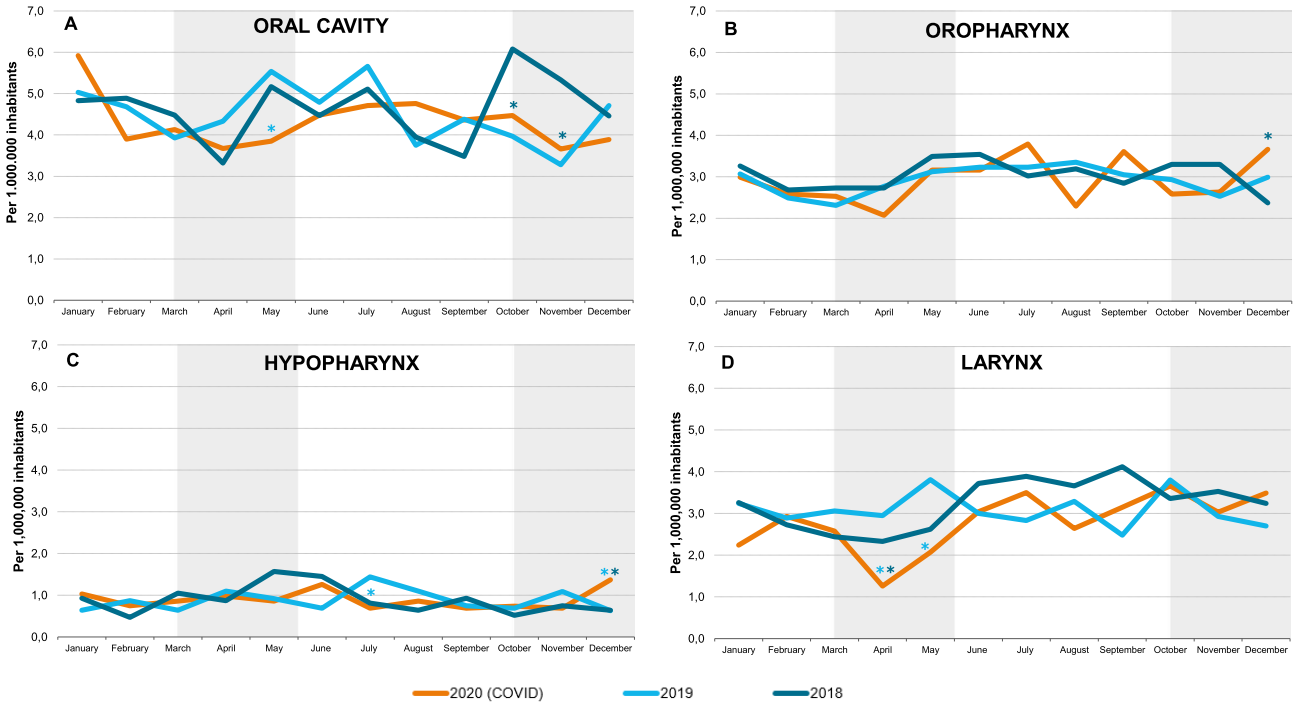

Fig. 2. Incidence (crude rate per 1,000,000) for oral cavity (A), oropharyngeal (B), hypopharyngeal (C) and laryngeal (D) carcinomas. The grey background blocks indicate the Netherlands' first and second COVID-19 wave and the accompanying lockdown measures (15 March – 1 June 2020, 14 October – 31 December 2020, respectively). The asterisks indicate a significant difference for 2018 vs. 2020 (COVID, dark blue asterisk) and for 2019 vs. 2020 (COVID, light blue asterisk).

Table 1
Baseline characteristics of HNC patients during the recovery months of the COVID-19 pandemic year in the Netherlands compared to the same period in 2018 and 2019.

	COVID-19 pandemic year	pre-COVID-19		*p*-value[a]
	1 June – 31 December 2020	*1 June – 31 December 2019*	*1 June – 31 December 2018*	
Characteristics	***n* = 1698**	***n* = 1635**	***n* = 1749**	
Age	66.4 ± 12.4	66.1 ± 12.0	66.3 ± 11.7	0.564
Sex				0.274
Female	584 (34.4%)	537 (32.8%)	575 (32.9%)	
Male	1114 (65.6%)	1098 (67.2%)	1174 (67.1%)	
Subsite				0.742
Oral cavity	463 (27.3%)	439 (26.9%)	486 (27.8%)	
Lip	66 (3.9%)	91 (5.6%)	80 (4.6%)	
Oropharynx	379 (22.3%)	370 (22.6%)	368 (21.0%)	
Nasopharynx	38 (2.2%)	41 (2.5%)	36 (2.1%)	
Hypopharynx	110 (6.5%)	111 (6.8%)	99 (5.7%)	
Larynx	393 (23.1%)	365 (22.3%)	438 (25.0%)	
Nasal cavity and paranasal sinus	74 (4.4%)	78 (4.8%)	77 (4.4%)	
Salivary gland	123 (7.2%)	98 (6.0%)	112 (6.4%)	
Unknown primary	51 (3.0%)	40 (2.5%)	53 (3.0%)	
Stage				**0.093**
I	505 (29.7%)	517 (31.6%)	546 (31.2%)	
II	295 (17.4%)	294 (18.0%)	297 (17.0%)	
III	254 (15.0%)	272 (16.6%)	308 (17.6%)	
IV (M0)	543 (32.0%)	472 (28.9%)	505 (26.9%)	
IVc (M1)	44 (2.6%)	38 (2.3%)	38 (2.2%)	
Unknown	57 (3.4%)	42 (2.6%)	55 (3.1%)	
Treatment modality				0.408
Surgery ± adjuvant therapy	724 (42.6%)	722 (44.2%)	794 (45.4%)	
Radiotherapy ± systemic therapy	784 (46.2%)	744 (45.5%)	784 (44.8%)	
Other therapies	43 (2.5%)	44 (2.7%)	31 (1.8%)	
No primary treatment	147 (8.7%)	125 (7.7%)	140 (8.0%)	

Values are presented as mean ± standard deviation or absolute numbers (column-percentage).
Bold values: statistical significance *p*-value <0.1.
[a] *p*-value representing first COVID-19 wave (2020) vs. pre-COVID (2018 and 2019 combined).

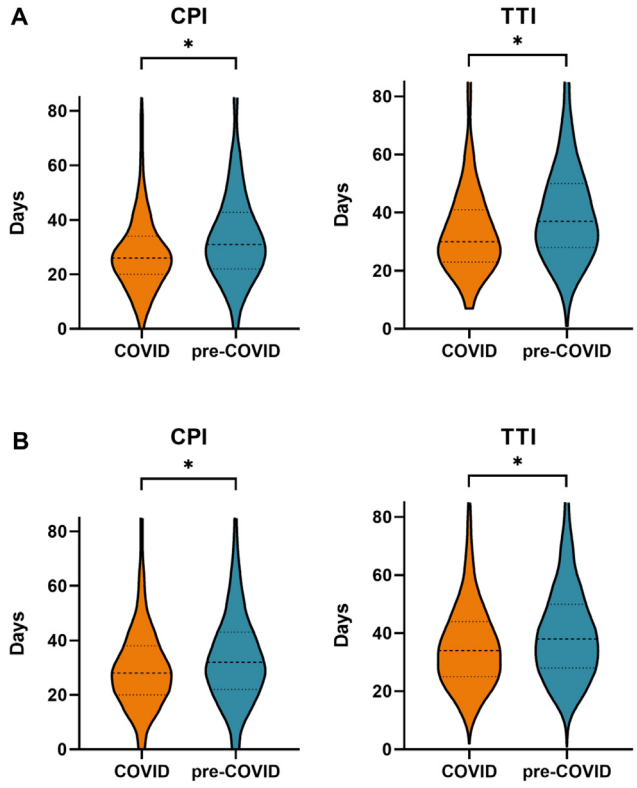

Fig. 3. Violin plot showing the Care Pathway Interval (CPI) and Time-to-Treatment Interval (TTI[‡]) during the first COVID-19 wave in 2020 (A) and during the recovery period in 2020 (1 June – 31 December, B) versus the same period in the two preceding years (2018 and 2019, pre-COVID). [‡]For TTI, patients with an interval of 0 days were excluded (COVID first peak n = 26 (7.1%) and n = 25 (5.7%) in recovery vs. n = 77 (7.6%) and n = 77 (6.4%) pre-COVID). The asterisk (*) indicates a significant difference between the COVID period (2020) and the corresponding periods in 2018 and 2019; p-value < 0.001. The size of the violin plot represents the number of individual data points, allowing more detailed interpretation of the distribution. The broken black line displays the median values, and the dotted lines display the 25th and 75th quartiles.

decrease of nearly 25%) than in the corresponding periods in 2018 and 2019, with incomplete recovery during the remainder of 2020. However, this fall applied mainly to the incidences of oral cavity and laryngeal carcinomas, and not to those of oropharyngeal and hypopharyngeal carcinomas. Whereas the distributions across the subsites and treatment modalities were similar to those in the two preceding years, a borderline significant trend towards increased stage IV tumours in 2020 was visible for the recovery period. Furthermore, the time-to-treatment intervals (CPI and TTI) were significantly shorter throughout the whole of 2020.

Incidence during COVID-19 vs. pre-COVID

This drop in incidence of HNC is consistent with earlier reports on cancer incidence during the COVID-19 pandemic [14], which reported a lower incidence in almost all cancer sites. As national screening programs were temporarily suspended to accommodate capacity for COVID-19 care, this effect was largest for breast, cervical and colorectal cancers [25]. To our knowledge, detailed incidence on HNC during the 2020 pandemic year has not been previously reported.

The lower reported incidence may be explained by factors related to patients, health care professionals and tumour-related symptoms. As a result of a general perception that the primary and secondary care systems were both overloaded with COVID-19 patients, especially during the first wave, patients with non-COVID symptoms may not have visited their GP due to moral concerns. Out of a fear of getting infected with SARS-CoV-2, patients may also have been anxious about entering healthcare facilities [13]. But as a majority of GPs' consultations were conducted online or by telephone rather than face to face, it is certain that physical examinations could not always take place, or only in a subsequent consultation.

The detection of oral cavity lesions was further restricted by the temporary closure of dental practices during the first wave of COVID-19. While it is possible that patients visited their dentist less often than in non-COVID times, little Dutch data supports this assumption. Nonetheless, a recent study reported that only 26.1% of Brazilian dental care practices maintained routine appointments during a lockdown [26]. As primary caregivers, dentists have an important screening function with regard to detecting oral cavity lesions. It is therefore possible that our assumption is supported by the observed decrease in oral cavity carcinoma. In future crises or circumstances with limited resources, patients should be encouraged to still seek medical help in case of alarming symptoms despite potential restrictions.

Another factor that may have contributed to the lower incidence of HNC is that their symptoms – such as coughing and hoarseness in laryngeal carcinoma – may resemble the first signs of COVID-19. During the first outbreak, COVID-19 testing capacities were too limited to allow testing of all those with symptoms, and people were advised to stay in quarantine. This may partly explain the significant decline in incidence of laryngeal carcinoma in April and May 2020.

That we found no decline in the incidence of oropharyngeal and hypopharyngeal carcinomas may be explained by the fact that many of these carcinomas are diagnosed when the tumour is already at an advanced stage, i.e. when the patient feels a more urgent need to seek medical help and the symptoms are more obvious for healthcare professionals.

The expected increase in incidence during the remaining months in 2020 was not observed. This incomplete recovery could be the result of an aftermath of the lower incidence during the first wave. Alternatively, it may be explained by not yet diagnosed HNC patients dying of or during COVID-19 [27]. The risk factors for severe consequences, including death, of COVID-19 largely overlap with risk factors for HNC (i.e. smoking, male sex). Furthermore, the presence of comorbidities and frailty is high in the HNC population [9], which could also contribute to the mortality risk.

Data on causes of death and shifts herein in the year of the corona-pandemic have recently become available for the Netherlands. The Central Bureau of Statistics (CBS) reports these numbers for the Netherlands and stated that the number of deaths was higher in the COVID-19 pandemic year and that their observations may point to an effect of substitution of cancer as cause of death by COVID-19, especially in elderly frail people [27]. Death due to COVID-19 was more common in men than women. As HNC patients are also more often men and a relatively high proportion of HNC patients could be considered frail [9], this group may have died more often of COVID-19. This may partly explain the lower number of diagnoses during the first wave and the observation that we did not observe an increased number of diagnoses thereafter. However, the magnitude of this effect remains unclear, and may not wholly explain the lower number of diagnoses since HNC is a rare disease.

Stage and treatment during the first year of the COVID-19 pandemic

During the first wave (15 March – 1 June), the distribution across the various tumour sites, stages and treatment modalities

Table 2
The categorized Care Pathway Interval (CPI) and Time-to-Treatment Interval during two periods within the COVID-19 year 2020 versus corresponding periods in the two preceding years (2018 + 2019). Intervals are categorized based on the Dutch norm in which 80% of the HNC patients are treated within 30 days.

Interval	*Treatment modality*	*Category*	1st COVID-19 peak *March 15th – June 1st 2020*	pre-COVID-19 *March 15th – June 1st 2018 + 2019*	*p*-value[†]	2nd half of COVID-19 year 2020 *June 1st – 31th December 2020*	2nd half pre-COVID-19 *June 1st – 31th December 2018 + 2019*	*p*-value[†]
CPI		*n*	*379*	*1044*		*1482*	*2979*	
	Total	0–30 days	256 (67.5%)	509 (48.8%)	<0.001	860 (58.0%)	1403 (47.1%)	<0.001
		>30 days	123 (32.5%)	535 (51.3%)		622 (42.0%)	1576 (52.9%)	
	Surgery	0–30 days	154 (80.6%)	313 (59.4%)	<0.001	494 (68.9%)	851 (56.8%)	<0.001
		>30 days	37 (19.4%)	214 (40.6%)		223 (31.1%)	648 (43.2%)	
	Radiotherapy	0–30 days	98 (53.9%)	184 (37.2%)	<0.001	345 (47.5%)	514 (36.4%)	<0.001
		>30 days	84 (46.2%)	311 (62.8%)		382 (52.5%)	898 (63.6%)	
TTI[‡]		*n*	*371*	*1019*		*1381*	*2730*	
	Total	1–30 days	187 (50.4%)	332 (32.6%)	<0.001	566 (41.0%)	851 (31.2%)	<0.001
		>30 days	184 (49.6%)	687 (67.4%)		815 (59.0%)	1879 (68.8%)	
	Surgery	1–30 days	104 (62.7%)	160 (35.2%)	<0.001	274 (44.2%)	433 (34.4%)	<0.001
		>30 days	62 (37.4%)	295 (64.8%)		346 (55.8%)	826 (65.6%)	
	Radiotherapy	1–30 days	81 (40.7%)	164 (30.3%)	0.007	303 (38.8%)	434 (28.3%)	0.006
		>30 days	118 (59.3%)	378 (69.7%)		478 (61.2%)	1098 (71.7%)	

[†] *p*-value representing COVID-19 pandemic year (2020) during the first peak (left columns) and recovery period (right columns) vs. corresponding periods in pre-COVID (2018 and 2019 combined), based on the chi-squared test. [‡] For TTI, patients with an interval of 0 days were excluded (COVID first peak *n* = 26 (7.1%) and *n* = 25 (5.7%) in recovery vs. *n* = 77 (7.6%) and *n* = 77 (6.4%) pre-COVID).

was not different from that in corresponding periods in 2018 and 2019. In the remaining months of 2020, however, a borderline significant trend towards higher proportion of stage IV tumours became apparent. The specific tumour growth rate of HNC is estimated at 1.8% per day and delays in presentation can easily lead to upstaging [28–30].

During the pandemic, overall recommendations were provided for the management of patients with HNC, including general guidelines on the timing of the start of oncological treatment [3,31]. Non-COVID care was compromised by the reduced availability of operating theatres for non-COVID care and by the overwhelming increase in the use of ICU capacity for COVID care. In addition, many care providers were temporarily transferred to COVID units. Despite the pressure on the healthcare system, oncological care for the patients who presented with HNC in 2020 seems unaffected. Especially in HNC, many patients receive primary or adjuvant radiation treatment. Despite the trend towards a possible stage shift to more advanced stage, no shift in treatment modalities was observed. This is in contrast with results of a recent study from the UK covering an overall cancer population, which suggested a shift from surgery to radiotherapy [32].

Time-to-treatment interval

Regardless of the first treatment modality, the CPI and TTI were significantly shorter during the first COVID-19 wave and thereafter. As timely treatment is of the utmost importance for HNC patients, time intervals within care pathways were nationally implemented as quality indicators. For most HNC centres, it was difficult to deliver treatment within the set and desired time intervals before the COVID period, which is generally explained by factors such as limited capacity and logistic challenges. Moreover, treatment intervals could have been extended by additional preoperative testing for SARS-CoV-2 [33]. However, during the first wave, overall recognition of the importance of a short time-to-treatment for patients with HNC seems to have led to HNC treatment prioritization. This, in combination with the lower volume of patients with HNC, may explain the significantly shorter CPI and TTI during the first wave of COVID-19.

This positive effect on time-to-treatment intervals sustained after the lockdown may be explained by the fact that once the waiting list has been shortened, the subsequent presenting patients profit. While returning to usual capacity and number of new patients, the previous equilibrium of demand and capacity is restored but with a shorter waiting list, leading to shorter time-to-treatment intervals.

Strengths and limitations

By including all patients with pathologically confirmed newly diagnosed primary HNC in the Netherlands, we ensured that this solid, population-based study could contribute to our understanding of the impact of the COVID-19 pandemic on the management of HNC care.

However, since the specific head and neck entities are relatively rare cancers, the numbers may not have been large enough to reflect subtle changes.

We are unlikely to have missed any delayed treatments: in all three years (2018–2020), the total duration of treatment for 99% of all patients lay within 140 days. Data was collected six months (approximately 180 days) after diagnosis, a timepoint that was chosen explicitly to ensure efficient and complete registration in one take. We did not investigate regional differences, even though COVID-19 prevalence differed, as COVID-19 patients were distributed over the whole country and HNC care in the Netherlands is centralized in only fourteen hospitals.

Conclusions

During the Netherlands' first COVID-19 wave, the incidence of HNC was nearly 25% less than that in the two preceding years. This decline in incidence was not compensated during the rest of 2020, in which a non-statistically significant trend towards higher staged tumours was observed.

Despite overloads in the healthcare system, the usual treatment could be delivered within a shorter time interval than usual, demonstrating that shorter time-to-treatment intervals are possible within the Netherlands' centralized HNC care setting where this oncological care is prioritized.

Data availability statement

Upon reasonable request to the corresponding author, the following can be made available: (1) the data dictionary, (2) syntaxes, and (3) de-identified participant data supporting our findings after signing a data access agreement.

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Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2021.12.005.

References

[1] World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19—11 March 2020, https://www.who.int/director-general/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020; 2020 [accessed February 16, 2021].
[2] Seth G, Sethi S, Bhattarai S, Saini G, Singh CB, Aneja R. SARS-CoV-2 infection in cancer patients: effects on disease outcomes and patient prognosis. Cancers (Basel) 2020;12:1–16. https://doi.org/10.3390/cancers12113266.
[3] Nagar H, Formenti SC. Cancer and COVID-19 — potentially deleterious effects of delaying radiotherapy. Nat Rev Clin Oncol 2020;17:332–4. https://doi.org/10.1038/s41571-020-0375-1.
[4] Burki TK. Cancer guidelines during the COVID-19 pandemic. Lancet Oncol 2020;21:629–30. https://doi.org/10.1016/S1470-2045(20)30217-5.
[5] Brindle ME, Gawande A. Managing COVID-19 in Surgical Systems. Ann Surg 2020;272:e1–2. https://doi.org/10.1097/SLA.0000000000003923.
[6] De Felice F, Polimeni A, Valentini V. The impact of Coronavirus (COVID-19) on head and neck cancer patients' care. Radiother Oncol 2020;147:84–5. https://doi.org/10.1016/j.radonc.2020.03.020.
[7] Zagury-Orly I, Schwartzstein RM. Covid-19 — A Reminder to Reason. N Engl J Med 2020;383:e12. https://doi.org/10.1056/NEJMp2009405.
[8] Bann DV, Patel VA, Saadi R, Gniady JP, Goyal N, McGinn JD, et al. Impact of coronavirus (COVID-19) on otolaryngologic surgery: Brief commentary. Head Neck, John Wiley and Sons Inc.; 2020. https://doi.org/10.1002/hed.26162.
[9] Bras L, Driessen DAJJ, Vries J, Festen S, Laan BFAM, Leeuwen BL, et al. Patients with head and neck cancer: Are they frailer than patients with other solid malignancies? Eur J Cancer Care 2020;29. https://doi.org/10.1111/ecc.v29.110.1111/ecc.13170.
[10] de Vries J, Bras L, Sidorenkov G, Festen S, Steenbakkers RJHM, Langendijk JA, et al. Frailty is associated with decline in health-related quality of life of patients treated for head and neck cancer. Oral Oncol 2020;111:105020. https://doi.org/10.1016/j.oraloncology.2020.105020.
[11] Fu TS, Sklar M, Cohen M, Almeida JR, Sawka AM, Alibhai SMH, et al. Is frailty associated with worse outcomes after head and neck surgery? A narrative review. Laryngoscope 2020;130:1436–42. https://doi.org/10.1002/lary.28307.
[12] NVM. Coronavirus: mondzorg staken, behalve bij spoed, https://www.nvmmondhygienisten.nl/nieuwsoverzicht-coronavirus/; 2020 [accessed April 28, 2021].
[13] Federatie Medisch Specialisten. Medisch specialisten maken zich zorgen over patienten die het ziekenhuis mijden, https://www.demedischspecialist.nl/nieuws/medisch-specialisten-maken-zich-zorgen-over-patiënten-die-het-ziekenhuis-mijden; 2020 [accessed September 28, 2020].
[14] Dinmohamed AG, Visser O, Verhoeven RHA, Louwman MWJ, van Nederveen FH, Willems SM, et al. Fewer cancer diagnoses during the COVID-19 epidemic in the Netherlands. Lancet Oncol 2020;21:750–1. https://doi.org/10.1016/S1470-2045(20)30265-5.
[15] Tang LV, Hu Y. Poor clinical outcomes for patients with cancer during the COVID-19 pandemic. Lancet Oncol 2020;21:862–4. https://doi.org/10.1016/S1470-2045(20)30311-9.
[16] Schutte HW, Heutink F, Wellenstein DJ, van den Broek GB, van den Hoogen FJA, Marres HAM, et al. Impact of time to diagnosis and treatment in head and neck cancer: a systematic review. Otolaryngol - Head Neck Surg (United States) 2020;162:446–57. https://doi.org/10.1177/0194599820906387.
[17] Schutte HW, den Broek GB, Steens SCA, Hermens RPMG, Honings J, Marres HAM, et al. Impact of optimizing diagnostic workup and reducing the time to treatment in head and neck cancer. Cancer 2020;126:3982–90. https://doi.org/10.1002/cncr.33037.
[18] Verdonck-de Leeuw IM, Jansen F, Brakenhoff RH, Langendijk JA, Takes R, Terhaard CHJ, et al. Advancing interdisciplinary research in head and neck cancer through a multicenter longitudinal prospective cohort study: the NETherlands QUality of life and Biomedical Cohort (NET-QUBIC) data warehouse and biobank. BMC Cancer 2019;19. https://doi.org/10.1186/s12885-019-5866-z.
[19] Addeo A, Friedlaender A. Cancer and COVID-19: Unmasking their ties. Cancer Treatment Rev 2020;88:102041. https://doi.org/10.1016/j.ctrv.2020.102041.
[20] Kuderer NM, Lyman GH. COVID-19, cancer, and consequences: where are we now? Cancer Invest 2020;38:431–5. https://doi.org/10.1080/07357907.2020.1812174.
[21] Licitra L, Keilholz U, Tahara M, Lin J-C, Chomette P, Ceruse P, et al. Evaluation of the benefit and use of multidisciplinary teams in the treatment of head and neck cancer. Oral Oncol 2016;59:73–9. https://doi.org/10.1016/j.oraloncology.2016.06.002.
[22] Kligerman MP, Vukkadala N, Tsang RKY, Sunwoo JB, Holsinger FC, Chan JYK, et al. Managing head and neck cancer patients with tracheostomy or laryngectomy during the COVID-19 pandemic. Head Neck, vol. 42, John Wiley and Sons Inc.; 2020, p. 1209–13. https://doi.org/10.1002/hed.26171.
[23] Nelson B. Covid-19 is shattering US cancer care. BMJ 2020;369. https://doi.org/10.1136/bmj.m1544.
[24] Schoonbeek RC, Vries J, Bras L, Plaat BEC, Dijk BAC, Halmos GB. Determinants of delay in the head and neck oncology care pathway: The next step in value-based health care. Eur J Cancer Care (Engl) 2021;30. https://doi.org/10.1111/ecc.v30.410.1111/ecc.13419.
[25] Dinmohamed AG, Cellamare M, Visser O, de Munck L, Elferink MAG, Westenend PJ, et al. The impact of the temporary suspension of national cancer screening programmes due to the COVID-19 epidemic on the diagnosis of breast and colorectal cancer in the Netherlands. J Hematol Oncol 2020;13. https://doi.org/10.1186/s13045-020-00984-1.
[26] Faccini M, Ferruzzi F, Mori AA, Santin GC, Oliveira RC, Oliveira RCGd, et al. Dental care during COVID-19 outbreak: a web-based survey. Eur J Dent 2020;14:S14–9. https://doi.org/10.1055/s-0040-1715990.
[27] Traag T, Hoogenboezem J (CBS). Doodsoorzaken 2000-2020: Verschuivingen in de meest voorkomende groepen doodsoorzaken tijdens de coronapandemie. https://www.cbs.nl/nl-nl/longread/statistische-trends/2021/doodsoorzaken-2000-2020; 2021 [accessed November 24, 2021].
[28] Žumer B, Pohar Perme M, Jereb S, Strojan P. Impact of delays in radiotherapy of head and neck cancer on outcome. Radiat Oncol 2020;15. https://doi.org/10.1186/s13014-020-01645-w.
[29] Dejaco D, Steinbichler T, Schartinger VH, Fischer N, Anegg M, Dudas J, et al. Specific growth rates calculated from CTs in patients with head and neck squamous cell carcinoma: a retrospective study performed in Austria. BMJ Open 2019;9:e025359. https://doi.org/10.1136/bmjopen-2018-025359.
[30] Metzger K, Mrosek J, Zittel S, Pilz M, Held T, Adeberg S, et al. Treatment delay and tumor size in patients with oral cancer during the first year of the COVID-19 pandemic. Head Neck 2021;43. https://doi.org/10.1002/HED.26858.
[31] Mehanna H, Hardman JC, Shenson JA, Abou-Foul AK, Topf MC, AlFalasi M, et al. Recommendations for head and neck surgical oncology practice in a setting of acute severe resource constraint during the COVID-19 pandemic: an international consensus. Lancet Oncol 2020;21:e350–9. https://doi.org/10.1016/S1470-2045(20)30334-X.
[32] Spencer K, Jones CM, Girdler R, Roe C, Sharpe M, Lawton S, et al. The impact of the COVID-19 pandemic on radiotherapy services in England, UK: a population-based study. Lancet Oncol 2021;22:309–20. https://doi.org/10.1016/S1470-2045(20)30743-9.
[33] Monroy-Iglesias MJ, Tagliabue M, Dickinson H, Roberts G, De Berardinis R, Russell B, et al. Continuity of cancer care: The surgical experience of two large cancer hubs in london and milan. Cancers (Basel) 2021;13:1597. https://doi.org/10.3390/cancers13071597.