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Original Research Article

A multi-centre survey reveals variations in the standard treatments and treatment modifications for head and neck cancer patients during Covid-19 pandemic

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ABSTRACT

Background: The onset of the COVID-19 pandemic necessitated rapid changes to the practice of head and neck oncology in UK. There was a delay between the onset of the pandemic and the release of guidelines from cancer societies and networks, leading to a variable response of individual centres. This survey was conducted to assess the pre-Covid-19 pandemic standard of practice for head and neck oncology patients and the treatment modifications introduced during the first wave of the pandemic in UK.

Methodology: The UK National Cancer Research Institute (NCRI) Head and Neck Clinical Studies Group initiated a multi-centre survey using questionnaire to investigate the effect on feeding tube practice, radiotherapy (RT) fractionation and volumes, use of chemotherapy in the neo-adjuvant, concurrent and palliative setting, the use of

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Chemotherapy
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immunotherapy in the palliative setting, access to radiology and histopathology services, and availability of surgical procedures.
Results: 30 centres were approached across UK; 23 (76.7%) centres responded and were included in the survey. There were differences in the standard practices in feeding tube policy, RT dose and fractionation as well as concurrent chemotherapy use. 21 (91%) participating centres had at least one treatment modification. 15 (65%) centres initiated a change in radical RT; changing to either a hypofractionation or acceleration schedule. For post-operative RT 10 centres (43.5%) changed to a hypofractionation schedule. 12 (52.2%) centres stopped neo-adjuvant chemotherapy for all patients; 13 (56.5%) centres followed selective omission of chemotherapy in concurrent chemo-radiotherapy patients, 17 (73.9%) centres changed first-line chemotherapy treatment to pembrolizumab (following NHS England's interim guidance) and 8 (34.8%) centres stopped the treatment early or offered delays for patients that have been already on systemic treatment. The majority of centres did not have significant changes associated with surgery, radiology, histopathology and dental screening.
Conclusion: There are variations in the standard of practice and treatment modifications for head and neck cancer patients during Covid-19 pandemic. A timely initiative is required to form a consensus on head and neck cancer management in the UK and other countries.

Background

Coronavirus disease 2019 (COVID-19) is highly contagious and caused by the SARS-CoV-2 virus that is mainly spread by respiratory secretions [1]. It was first recognised following an outbreak of the disease in December 2019 in Wuhan, China. It was declared as a global pandemic by the World Health Organisation on 11th March 2020 [2]. Retrospective evidence produced early in the pandemic from China indicated that cancer patients, including those receiving treatment for cancer were at increased risk of serious COVID-19 morbidity, including the need for ventilator support or death [3]. However, later studies including a larger number of patients have shown that the mortality for cancer patients with COVID-19 appears to be principally driven by the patients' other co-morbidities, age and gender rather the use of anti-cancer treatment [4]. Nevertheless, there may be a difference in patients with haematological cancers since some of these patients with SARS-CoV-2 infection have worse outcomes compared with both the general population with SARS-CoV-2 and patients with haematological malignancies without COVID-19 while the immune signatures of SARS-CoV-2 positive solid cancer patients resembled those for SARS-CoV-2 positive non-cancer patients [5]. This may be related to some of the patients with B cell-related haematological cancers have continued viral shedding without developing antibodies for a prolonged period [6].

Since the outbreak of COVID-19, oncology departments have had to consider risk mitigation strategies for patients both because of reduced availability of radiographers and chemotherapy nurses due to sickness, self-isolation or staff redeployment and concerns regarding the possible consequences of anticancer treatment or of potential exposure of patients to risks of viral transmission during their visits to the hospital [7]. The outcomes for patients with head and neck squamous cell carcinoma (HNSCC), depend on a number of factors, not least HPV status [8]. Recent data suggest 84.6% 5-yr overall survival [9] and 97.5% 2-yr overall survival [10] for better prognosis HPV-driven disease whilst mortality is much higher for high-risk HPV-negative tumours with a 3-year overall survival of 57.1% (8). HNSCC poses particular problems due to frequent visits required for a course of radical chemo-radiotherapy. Moreover, there is a significant risk of aerosol generation during diagnostic workup for patients with HNSCC, and there is evidence from China, Italy, and Iran, of increased transmission rates to otolaryngologists[11]. A number of guidelines have been published from both surgical and oncology networks at institutional, national and international levels to assist clinicians in the safe delivery of services based on the new challenges faced [12–16].

The American Society of Radiation Oncology (ASTRO) and the European Society for Radiotherapy and Oncology (ESTRO) published practice recommendations for radiation oncologists involved in the care of head and neck cancer patients in April 2020 [12]. The aim of the current study, initiated by NCRI Head and Neck Clinical studies group, was to survey UK head and neck oncologists regarding both standard practice pre-pandemic and the treatment modifications introduced for head and neck cancer patients during the first wave of the COVID-19 pandemic.

Materials and methods

The UK NCRI Head and Neck Clinical Studies Group initiated a multi-centre survey by distributing a Microsoft excel (with Microsoft word version) questionnaire containing 21 questions to head and neck clinical oncologists at different UK centres to assess pre-pandemic standard treatments and the treatment/practice modifications introduced. The questionnaire was designed to investigate the effect of the first wave of the pandemic on prophylactic or reactive use of feeding tubes, access to radiology and histopathology services, availability of diagnostic and therapeutic surgical procedures, radiotherapy fractionation and volumes, use of chemotherapy in the neo-adjuvant, concurrent and palliative setting and the use of immunotherapy in the palliative setting.

The questionnaire was sent out in July to September 2020 to a total of 30 centres across UK and all replies were collected by December 2020. This survey covered the period between February 2020 to July 2020 which is the period following the first wave of COVID-19 pandemic. The questionnaire included a total of 9 main domains with further questions in each domain as evident in the appendix. The survey aimed to investigate changes in patterns of practice across head and neck oncology units in general, and did not specify response stratification by primary site or histological subtype. Therefore, whilst the majority of data presented pertain to patients with HNSCC, changes in practice for salivary gland tumours, and cutaneous cancers of the head and neck are also represented.

Results

Thirty centres were approached and twenty three (76.7%) oncologists from different cancer centres responded and participated in the survey including those from Guys Cancer Centre (London), Leeds Cancer Centre, Beatson Glasgow Centre, Imperial College Healthcare NHS Trust (London), Weston Park Cancer Centre (Sheffield), Royal Marsden Hospital (London & Sutton), Clatterbridge Cancer centre (Liverpool), Kent Oncology Centre West, Kent Oncology Centre East, Oxford University Hospitals, Aberdeen Royal Infirmary, Norfolk & Norwich University Hospitals NHS Foundation Trust, Queen Elizabeth Hospital (QEH) (Birmingham), The Royal Wolverhampton NHS Trust, Castle Hill Hospital (Cottingham), Nottingham University Hospitals, Lingen Davies Cancer Center (Royal Shrewsbury Hospital), Torbay Hospital (Torquay), Musgrove Park Hospital (Taunton), Royal United Hospital (Bath), Derriford Hospital (Plymouth), Edinburgh Cancer Centre and Northampton General Hospital.

21 (91%) centres had at least one treatment modification and this commenced in March 2020 during the peak of the first wave. 9/23

(39.1%) applied changes to standard practice for 2 months, 8/23 (34.8%) for 3 months, 3/23 (13.0%) for 4 months and 1/23 (4.3%) for 7 months (change in radiotherapy fractionation maintained until October 2020). All centres initiated modifications based on the increase in incidence and the risk of complications and mortality from exposure to SARS-CoV-2 infection. Most clinicians attempted to reduce the number of visits and thus reduce the risk of the patients getting infected with the virus. Although two centres did not report any treatment modification during this period, one of the centres adopted a watch and wait approach on new systemic treatment and the other centre used pembrolizumab as 1st line systemic treatment for recurrent or metastatic HNSCC in the palliative setting following NHS England's Interim Guidance on pembrolizumab [17]. The two centres with no modifications reported low incidence of Covid-19 infection in the geographical area covered by the unit surveyed and thus did not see any need for treatment modifications

Feeding tube

We found that the feeding tube practice for head and neck cancer patients undergoing radical radiotherapy treatment varies across UK. Most centres (18/23; 78.3%) reported the use of elective/prophylactic percutaneous endoscopic gastrostomy (PEG) or radiologically inserted gastrostomy (RIG) for most patients or specifically for patients undergoing bilateral neck irradiation and/or concurrent chemotherapy. A smaller number of cancer centres (5/23; 21.7%) reported a reactive policy of nasogastric/nasojejunal tube (NGT/NJT) inserted during radiotherapy when patients experience difficulty in swallowing with elective RIG/PEG being reserved for those with pre-existing or deemed to have imminent swallowing or aspiration problems during radiotherapy. Eight (34.8%) centres changed their feeding tube practice during Covid-19 pandemic: two centres (8.7%) changed their practice from reactive to elective feeding tube, five centres (21.7%) changed from elective/prophylactic PEG/RIG to reactive NGT (three centres reported that this was due to reduced capacity for the procedure) and one centre (4.3%) changed from prophylactic gastropexy to PEGs due to restrictions in local endoscopy service (table 1 and Fig. 1)

Radiotherapy volumes and fractionation

The survey demonstrated variation in the standard primary radical radiotherapy fractionation used for head and neck cancer patients across the cancer centres. The 70 Gy/35 fractions/7 weeks (70 Gy/35#) fractionation is regarded as gold standard worldwide and is more commonly used at many cancer centres throughout the world. In this survey, it is still used at 6/23 (26.1%) participating centres while the majority of the centres (17/23;73.9%) have adopted 65 Gy/30 fractions/6 weeks (65 Gy/30#). One centre uses 70 Gy/35 fractions for patients undergoing concurrent chemoradiation but uses 65 Gy/30 fractions for patients undergoing radical radiotherapy alone.

During the Covid-19 first wave peak, fifteen (65%) centres initiated a change in radical radiotherapy fractionation schedule (Table 2 and Fig. 2). For those centres that where 70 Gy/35# was standard, this fractionation continued to be used for some younger and fit patients while selected patients (including those older and those with co-morbidities) received 65 Gy/30#, DAHANCA [18] (68 Gy/34# x 6/week) instead of concurrent chemoradiation or 55/20# (small volume). For those centres that use 65 Gy/30# as their standard fractionation, treatment modification included 55 Gy in 20# (either all or selected patients such as those with co-morbidities or older patients) or 50 Gy/15–16# (small volumes) and 3 centres used 68 Gy/34# x 6 fractions per week (DAHANCA) instead of chemoradiation [18] . For early larynx SCC T1/T2N0M0, 55 Gy/20# is the standard fractionation but during Covid-19 pandemic, one centre used 50 Gy/16# as an option for T1 larynx SCC and another centre used 50 Gy/15# or 50 Gy/16#.

For postoperative radiotherapy (PORT), the standard practice for UK centres was generally consistent, using 60 Gy/30# (64–66 Gy/32–33# for high risks such as positive margin or extracapsular spread at some centres). Ten (43.5%) centres reported changing their standard PORT fractionation to 50 Gy or 55 Gy in 20# (either for all patients or for selected patients such as those with co-morbidities or older patients and

Table 1
Feeding tube practice for head and neck patients undergoing radical radiotherapy across UK.

Oncology centres	Standard practice	During COVID-19
Guys Cancer Centre; London	Reactive	Prophylactic
Leeds Cancer Centre; Leeds	Therapeutic RIG in patients with unsafe swallowing. Prophylactic RIG or reactive NG option for the remaining patients with safe swallowing (patients' decision)	No change
Beatson Glasgow Centre; Glasgow	Reactive NG tube if G3 dysphagia	No change
Imperial College Healthcare NHS Trust; London	Prophylactic for bilateral RT and ipsilateral RT with concurrent chemotherapy. Reactive RIG for lateralised patients receiving RT alone	Reactive for all patients
Weston Park Cancer Centre; Sheffield	Prophylactic gastrostomy insertion prior to CRT or in patients struggling with swallow pre-RT/CRT	No change
Royal Marsden Hospital; London and Sutton	Reactive	Prophylactic
Clatterbridge Cancer centre; Liverpool	Prophylactic for CRT patients	No change
Kent Oncology Centre-East (Canterbury)	Prophylactic gastropexy	PEGs (restrictions to endoscopy)
Kent Oncology Centre – West (Maidstone)	Prophylactic	Reactive NJT (lack of access to PEGs)
Oxford University Hospitals; Oxford	Prophylactic	Reactive NGs (reduced capacity)
Aberdeen Royal Infirmary; Aberdeen	Reactive NG feeding	No change
Norfolk & Norwich University Hospitals NHS Foundation Trust Norwich	Prophylactic for CRT bilateral neck or any swallowing issues	Reactive
Queen Elizabeth Hospital; Birmingham	Reactive	No change
The Royal Wolverhampton NHS Trust; Wolverhampton	Prophylactic	Some changed to reactive (reduced capacity)
Castle Hill Hospital; Cottingham	Prophylactic for radical CRT to bilateral neck or if indicated by dietician review	No change
Nottingham University Hospitals; Nottingham	Prophylactic for CRT patients	No change
Lingen Davies Cancer Centre; Shrewsbury	Prophylactic PEG for bilateral neck	No change
Torbay Hospital; Torquay	Prophylactic for bilateral neck irradiationReactive NG tube for others	No change
Musgrove Park Hospital; Taunton	Prophylactic for bilateral treatment	No change
Royal United Hospital; Bath	Prophylactic RIG for (C)RT andbilateral radical radiotherapy treatment unless limited volume RT alone	No change
Derriford Hospital; Plymouth	RIGs/PEGs for bilateral neck irradiation or unilateral with chemo	No change
Edinburgh Cancer Centre; Edinburgh	Prophylactic for CRT patients and selective big volume RT patients	No change
Northampton General Hospital; Northampton	Prophylactic	No change

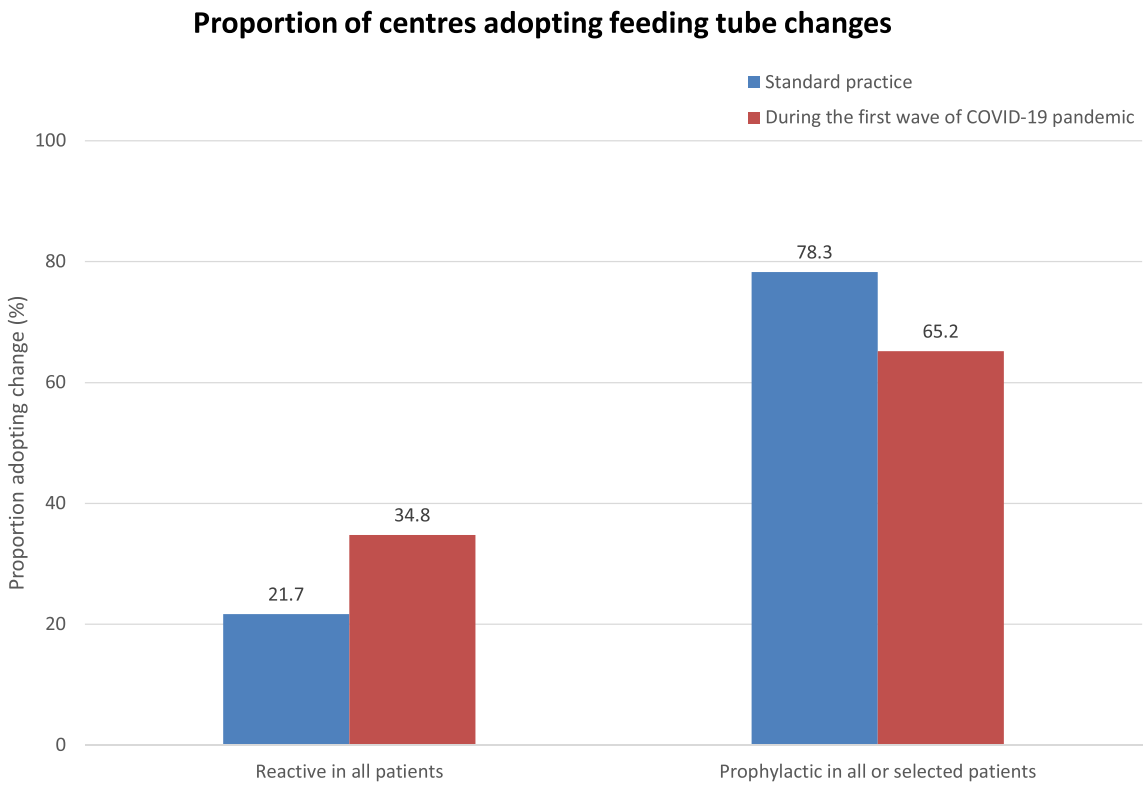

Fig. 1. Changes to feeding tube practice following the first wave of COVID-19 pandemic. *Selected patients*: bilateral neck radiotherapy or ipsilateral with concurrent chemotherapy. 2 centres (8.7%) switched from reactive to prophylactic feeding tube insertion and 5 centres (21.7%) changed from prophylactic to reactive NGT tube. One centre (4.3%) changed from prophylactic gastropexy to PEGs. 15 centres (65.2%) had no change in practice.

those undergoing small volume and unilateral radiotherapy treatment at some centres) (Table 2). In addition to using 50–55 Gy/20# for PORT, one centre stated that they discussed pros and cons of not having PORT in intermediate risk patients with comorbidities and omission of chemotherapy and use of PORT +/- boost in high-risk patients. One centre used 60 Gy/30# with simultaneous integrated boost (SIB), 65 Gy/30# to high-risk volume (in place of concurrent chemoradiation) while using 50 Gy/20# for small volumes (Table 3).

For palliative radiotherapy fractionation, four (17.4%) centres have reported a change with three centres avoided using radiotherapy longer than 1 week (e.g. 25 Gy/5#, 20 Gy/5# or 8 Gy/1#) and one centre changed from 45 Gy/15# to 27 Gy/6#/twice weekly. One centre reported no change for most patients but considered 27 Gy/6#/twice weekly if needed. Most other centres did not change palliative fractionation and used 20 Gy in 5 fractions and/or 8 Gy in 1 fraction while 3 centres continued to use 14 Gy/4# (twice a day and at least 6 h apart, for 2 consecutive days, repeated at 4 weekly intervals for a further two courses if no disease progression) [19].

Only three centres (13%) reported changing their radiotherapy delineation protocols. One centre adopted the international consensus target delineation guidelines (5 + 5 margin) [20] for primary and nodal GTV in selected patients; those with easily identified tumours in CT planning scan and those with MRI planning scan) and selected cases had modified target volume delineation including omitting contralateral nodal irradiation with possible reduction in ipsilateral nodal irradiation to include only the level adjacent to involved nodes except retropharyngeal node and avoided irradiation to the lung apices. A further centre changed the volume delineation for elderly high risk PORT patients by offering unilateral rather than bilateral neck radiotherapy, in selected cases, in an attempt to reduce the overall burden of acute toxicity, and the need for hospital admission. At one centre, standard delineation was carried out in most patients although small adaptation was applied to reduce the extent of prophylactic level 4 neck nodal volumes inferiorly to minimise irradiation to lung apices and prophylactic irradiation to the higher retropharyngeal (RP) lymph nodes was excluded where the risk of spread was low. In addition, unilateral treatment was considered in moderate risk or frail patients

Systemic treatment:

Neo-adjuvant chemotherapy:

Neoadjuvant chemotherapy is usually only given to selected patients at most cancer centres including those with nasopharyngeal cancer or those with heavier disease burden or positive nodal disease. During the COVID-19 pandemic, twelve (52.2%) centres stopped giving neo-adjuvant chemotherapy treatment to all patients and 8 (34.8%) centres were giving neo-adjuvant chemotherapy to very exceptional cases including young patients, those with significant disease related symptoms or those with nasopharyngeal cancers. If given, it was reported that neoadjuvant treatment was given either with dose reduction (75% Cisplatin), 2 drugs (instead of 3 drugs combination like docetaxel, cisplatin and 5FU chemotherapy) and/or with GCSF cover. One (4.3%) centre was giving neo-adjuvant chemotherapy with dose reduction (75% Cisplatin). Two (8.7%) centres reported no change in the neo-adjuvant chemotherapy standard practise (Fig. 3a).

Concurrent chemotherapy. One (4.3%) centre omitted chemotherapy for all patients. Thirteen (56.5%) centres omitted chemotherapy in selected cases (e.g. > 60 or if DAHANCA radiotherapy fractionation is used or after discussion with selected patients). At one of these centres patients were given the option to omit following detailed discussion of risk versus benefit. All but 2 patients at this centre chose to carry on with concurrent chemotherapy. Three (13%) centres changed cisplatin to carboplatin for all patients, whereas one centre changed to carboplatin for only selected patients. Two (8.7%) centres changed the cisplatin schedule from 3 cycles to 2 cycles (standard radiotherapy fractionation

Table 2
Radical radiotherapy fractionation (primary or PORT) for head and neck patient across UK.

Oncology centres	Standard practice	During COVID-19
Guys Cancer Centre	Primary:65 Gy/30# PORT: 60 Gy/30#	Primary: 55 Gy/20#/50 Gy/ 15–16# (small volume); PORT: 50 Gy/20#
Leeds Cancer Centre	Primary: 70 Gy/35#/ 7wks (For RT only 65 Gy/30#/6 weeks) PORT: 60–66 Gy/ 30–33#	Primary: 65 Gy/30# PORT: No change
Beatson Glasgow Centre	Primary:65 Gy/30# high-risk, 54 Gy/30# low-risk; PORT: 60 Gy/30#	No change
Imperial College Healthcare NHS Trust	Primary:65 Gy/30#; PORT: 60 Gy/30# Small field larynx: 55 Gy/20#	55 Gy/20# (>80 or significant comorbidities) or deferred during peak
Weston Park Cancer Centre	Primary:70 Gy/35# PORT: 60–66 Gy/ 30–33#	Mostly no change. If small volume or DAHANCA (68 Gy/ 34# x 6/ week)
Royal Marsden Hospital	Primary: 65 Gy in 30# PORT: 60 Gy/30#	No change
Clatterbridge Cancer centre	Primary:70 Gy/35# PORT: 60 Gy/30#	Primary: Selected patients: 65 Gy/30#; Smaller volumes: 55 Gy/20#; T1 Larynx: 50 Gy/16# option; PORT: Patient discussion in intermediate risk patients with comorbidity. High-risk patients discuss omission of chemotherapy and use RT +/- boost; Consider use of 4-week regime 50–55 Gy in 20#
Kent Oncology Centre; East	Primary:70 Gy/35# PORT: 66 Gy/33#	Primary: 70 Gy/35# for young patients; otherwise 55 Gy/20#; PORT: 55 Gy/20#
Kent Oncology Centre; West	Primary:70 Gy/35# PORT: 60–66 Gy/ 30–33#	Primary:55 Gy/20# (selected patients); PORT: 55 Gy/20#
Oxford University Hospitals	Primary: 65 Gy/30# PORT: 60 Gy/30#	No change (used 55 Gy/20# in 4–5 patients)
Aberdeen Royal Infirmary	Primary: 65 Gy/30# (Nasopharynx 70 Gy/ 33#, early glottis 55 Gy/ 20#) PORT: 66–60 Gy/ 33–30#	No change
Norfolk & Norwich University Hospitals	Primary: 65 Gy in 30# PORT: 60–66 Gy/30#	Primary: 55 Gy/20# in very selected elderly population; DAHANCA 68/34#/6 weeks per week when no chemo; PORT: 50 Gy/20# in very selected elderly population
Queen Elizabeth Hospital	Primary: 65 Gy in 30# PORT: 60–65 in 30#	55 Gy/20# discussed as alternative to standard particularly ≥ 60 years
The Royal Wolverhampton NHS Trust	Primary: 65 Gy/30# weekly PORT: 60 Gy/30#	No change
Castle Hill Hospital	Primary: 66/60/54 in 30# (SIB ARC) PORT: 60/63 Gy/30#	No change
Nottingham University Hospitals	Primary: 70 Gy in 35# PORT: 66 Gy/33# if ECE or R1 (weekly platinum), 60 Gy in 30# for no high-risk features	Primary: 65 Gy/30# PORT: No change
Lingen Davies Cancer Centre	Primary: 65 Gy/30# PORT: 60 Gy/30#	Primary: 55 Gy/20# for patients felt to be high risk of covid-19; 50 Gy/16# small volume larynx. PORT: considered 50/20# for concerned patients but almost all had 60 Gy/30#
Torbay Hospital, Torquay	Primary: Both 65 Gy/ 30# and 70 Gy/35#. PORT:66 Gy (residual disease/ECE), 60 Gy (post-op bed), 54 Gy (low risk untreated neck)/30–33#	No change
Musgrove Park Hospital, Taunton	Primary:65 Gy/30# PORT: 60 Gy/30#	Primary: 55 Gy/20# small volume treatments in those with co-morbidities; PORT: 50 Gy/20# in some small volume unilateral treatments
Royal United Hospital	Primary: 65 Gy/30# PORT: 60 Gy/30#	Primary: 55 Gy/20# (small volumes), 68 Gy/34# x 6/week (DAHANCA in place of CRT); 65 Gy/30# larger volumes (not chemo eligible, age or co-morbidities); PORT: 50 Gy/ 20# (small volumes); 60 Gy/ 30# with SIB; 65 Gy/30 # to high-risk volume (in place of CRT)
Derriford Hospital	Primary:65 Gy/30# PORT: 60 Gy/30# if no ECS and 65 Gy/30# if ECS	Primary: 55 Gy/20# if small volumes (but most continued at 65 Gy/30#); PORT: 50 Gy in 20 # on occasion (but most continued as normal)
Edinburgh Cancer Centre	Primary: 65 Gy/30# PORT: 60 Gy/30#, consider boost to 65 Gy if residual disease/ECE.	No change
Northampton General Hospital	Primary: 65 Gy in 30# PORT: 60 Gy in 30#	No change

at these centres was 70 Gy/35#; one centre gave GCSF cover and one centre gave reduced dose). One (4.3%) centres changed treatment to week 1 and week 5 instead of three weekly, one (4.3%) centre changed from three weekly cisplatin to weekly and one (4.3%) centre omitted cycle 2 of treatment for majority of patients already on concurrent chemoradiation. One (4.3%) centre changed cisplatin to 75% of dose with the same schedule and three (13.0%) centres did not change treatment (Fig. 3a).

New palliative systemic treatment

Seventeen (73.9%) centres changed 1st line palliative systemic chemotherapy treatment to pembrolizumab for recurrent or metastatic HNSCC following NHS England's interim guidance and approval of pembrolizumab for eligible patients. Five centres (21.7%) followed either a 'watch and wait' approach or delayed all referrals. One (4.3%) centre did not change palliative 1st line treatment practice (Fig. 3a).

Existing systemic treatment

Ten (43.5%) centres did not change chemotherapy treatment for patients on treatment, eight (34.8%) centres stopped the treatment early or offer delays during lockdown, one (4.3%) centre reduced dose to 75% and stopped cetuximab, one (4.3%) centre changed cetuximab from weekly to two weekly. One (4.3%) centre stopped only 3rd line chemotherapy with two (8.7%) centres decision was taken on individual basis (Fig. 3a).

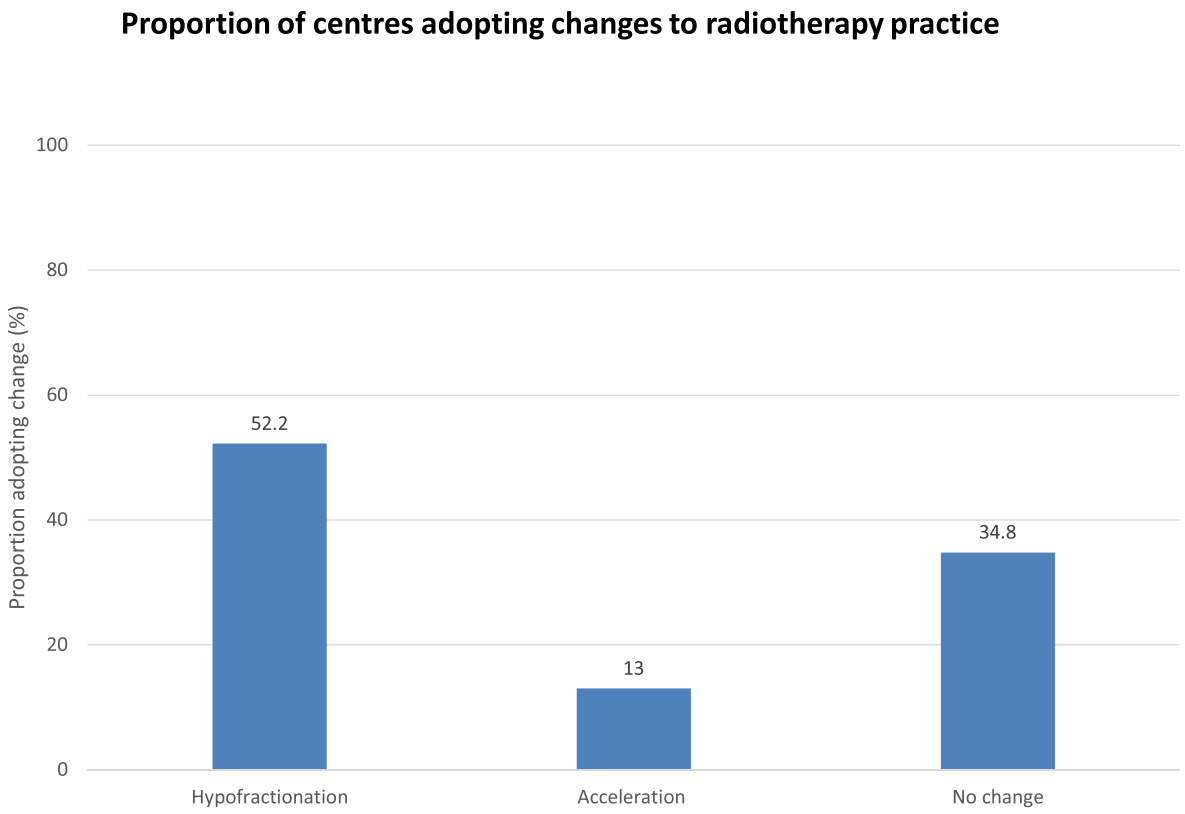

Fig. 2. Changes to primary radiotherapy fractionation schedule following the first wave of COVID-19 pandemic. *Hypofractionation*: Reduction in fraction number and increase in fraction size for some patients, relative to standard pre-covid protocol; *Acceleration*: DAHANCA protocol (68 Gy/34#/6 weeks); 2 of the 3 centres in the acceleration group were offering the option of hypofractionation as well.

Second-line immunotherapy (nivolumab) post platinum chemotherapy progression

Twelve (52%) centres changed nivolumab treatment from 2-weekly to 4-weekly. Nine (39%) centres did not make any change to nivolumab treatment (one centre changed some to 4 weekly based on individual discussion). Two (8.7%) centres offered a treatment break during lockdown (Fig. 3a).

Surgery

Fourteen (64.8%) centres had no change in surgical practice. Seven (30.4%) centres had changes in selected cases where it was decided to deliver primary radiotherapy instead of surgery due to various reasons including limited access to theatre or intensive care unit (Fig. 3b). One centre (4.3%) did not proceed to surgery in high-risk cases with low chance of cure which might have been attempted before Covid-19 pandemic and these patients were not treated radically. At one centre (4.3%), the maxillofacial team undertook local resection and omitted neck dissections in cN0 high risk patients and replaced with close surgical FU instead. Since the trial recruitment for PATHOS (Post-operative Adjuvant Treatment for HPV-positive Tumours) was suspended nationally during this time, patients who would have been offered the trial were treated with definitive radiotherapy instead for the duration for the trial as per the standard of care at their cancer centres.

Radiology

The radiologist assistance during target volume contouring remained the same in eighteen (78%) centres and it was not applicable in 5 centres (22%). Moreover, twelve (52.2%) centres had the same capacity for scans. Ten (43.5%) centres performed only urgent scans and one (4.3%) centre had delays in imaging. Sixteen (70%) centres had no delays in reporting; eight (30%) centres had only minor delays in reporting (Fig. 3b).

Histopathology

Twenty-two (95.7%) centres had no change in histopathology reporting while only one (4.3%) centre has some delays in reporting (Fig. 3b).

Dental screening

Nineteen centres (82.6%) had no change in baseline dental screening; four (17.4%) centres had some changes with one (4.3%) having telephone-based prevention advice and two centres (8.7%) stopping their service. Ten (43.5%) centres had no change in post-treatment dental monitoring; in ten (43.5%) centres their treatment was cancelled or deferred; two (8.7%) centres changed to telephone consultation and 1 centre (4.3%) moved all patients to a different department as the local dental department closed.

COVID-19 screening pre-treatment and other changes

Twelve (52.2%) centres performed pre-treatment COVID swab test since the pandemic and four of these centres reported doing swabs weekly during treatment. Most centres have introduced several safety measures including personal protective equipment (PPE) use, reducing face to face consultation and increasing the use of video or telephone consultation, limitation of visitors to cancer centres, temperature check for patients and visitors, symptomatic and/or Covid-19 positive patients to have either treatment delay and/or to have treatment at a separate machine or the end of the day if it was deemed absolutely necessary to

Table 3
Concurrent chemotherapy schedule for head neck patients on chemo-radiotherapy across UK.

Oncology centres	Standard practice	During COVID-19
Guys Cancer Centre	3 weekly cisplatin	Omitted for all patients
Leeds Cancer Centre	3 weekly cisplatin; 3 cycles (35#)	2 cycles (30#)
Beatson Glasgow Centre	3 weekly cisplatin	75% dose
Imperial College Healthcare NHS Trust	3 weekly cisplatin	Carboplatin substituted cisplatin
Weston Park Cancer Centre	3 weekly cisplatin	Omitted in some patients if > 60yrs of age and if DAHANCA schedule used (68 Gy/34#)
Royal Marsden Hospital	Week 1 & 4 cisplatin; 100 mg/m2	Carboplatin substituted cisplatin
Clatterbridge Cancer centre	3 weekly cisplatin (35#)	2 cycles (30#); reduced dose
Kent Oncology Centre; East	Weekly cisplatin	No omission or change to carboplatin. Change cisplatin to weeks 1 and 5
Kent Oncology Centre; West	3 weekly cisplatin	Considered omitting in > 60 - when given changed from 3 weekly to week 1 and week 5 with GCSF cover
Oxford University Hospitals	3 weekly for PS0 patients, 40 mg/m2 weekly for other eligible patients risk of toxicity	Omission in selected cases after discussion with patient
Aberdeen Royal Infirmary	3 weekly cisplatin	No change
Norfolk & Norwich University Hospitals	Weekly cisplatin	Omitted in selected cases (opted for DAHANCA instead)
Queen Elizabeth Hospital	Weekly cisplatin	For < 60 considered changing cisplatin to 3 weekly carboplatin. Omission of chemotherapy considered in 60–70 years
The Royal Wolverhampton NHS Trust	Weekly cisplatin (3 weekly is also in formulary)	Omission of chemotherapy discussed for patients 60–70 and avoided in some patients balancing risk and benefit. No change of cisplatin to carboplatin or schedule
Castle Hill Hospital	Weekly cisplatin (except nasopharynx 3 weekly)	No change; but patients were given the option to omit following detailed discussion of risk vs benefit.
Nottingham University Hospitals	Weekly or 3 weekly	Omitted for some patients > 60 where benefit felt to be smaller; change of cisplatin to carboplatin for most patients given concurrent chemo but no change of schedule change
Lingen Davies Cancer Centre	Weekly cisplatin	Omission for some patients; no change of cisplatin to carboplatin or schedule
Torbay Hospital, Torquay	Weekly cisplatin	Omission in selected cases after discussion with patient; continue weekly cisplatin (not changed to carboplatin)
Musgrove Park Hospital, Taunton	3 weekly cisplatin	Omission in a small number of patients age > 60, 3 weekly changed to weekly but no change of cisplatin to carboplatin
Royal United Hospital	3 weekly cisplatin	Second cycle of concurrent chemo omitted for majority of patients already on CRT after discussion regarding risks/benefits; no change of cisplatin to carboplatin or schedule change
Derriford Hospital	Weekly cisplatin	Only omitted concurrent chemotherapy in a few patients after discussion of the national guidance and most patients continued to receive concurrent treatment as normal
Edinburgh Cancer Centre	Week 1 & 5 cisplatin	No change
Northampton General Hospital	Weekly cisplatin	No change

have treatment.

Discussion

The onset of the COVID-19 epidemic necessitated swift changes to the practice of head and neck oncology. This was facilitated by guidelines produced by a range of specialist professional organisations, as well as by guidance from central authorities such as NHS England, and included changes to rigid commissioning and funding rules including those for the Cancer Drugs Fund (12–16). However, there was an inevitable delay between the onset of the pandemic and these publications, let alone any pertinent clinical data to guide decision making in the era of COVID-19. Therefore, as case numbers increased exponentially throughout the country in March and April, individual cancer centres had to make decisions about how standard treatment protocols should, or should not, be amended in the absence of any guidelines or consensus. We were particularly interested in the changes introduced following the first wave when oncologists were uncertain what to do, having never encountered this previously. We covered the survey between February to July 2020 since most centres had resumed normal practice by the end of June 2020 when the Covid-19 restrictions started to ease in the UK (although the survey found out that one centre had changes lasted until October 2020).

That individual centre responses should vary was inevitable. Not only were there significant differences in rates of COVID-19 infection, hospitalisation and pressures on ITU beds across the country during this time, but centres faced heterogeneous practical challenges such as the physical layout of departments, size of waiting rooms, availability of slots for systemic therapy, and staffing issues, in addition to the pressures on allied services such as surgery and radiology as seen in our data. Therefore, it is reasonable to suppose that each surveyed centre was faced with its own unique set of specific challenges, within the context of the broader national response to the pandemic.

Despite this, there are some clear trends in the ways in which clinicians responded to the challenges of COVID-19. With regards to radiotherapy fractionation schedules, 2 interesting themes emerge. Firstly, that 65 Gy in 30 fractions over 6 weeks has been widely accepted across the country as standard practice, with 17/23 surveyed centres (73.9%) reporting that this schedule was a standard protocol option before the onset of the pandemic. In contrast, 2 Gy per fraction schedules (70/35) were used by only 6/23 (26.1%) of centres. Secondly, we observed a clear trend towards centres increasing dose per fraction, and/or reducing overall treatments during the pandemic. Fifteen of 23 surveyed centres (65.2%) changed practice to incorporate a schedule that did at least one of these things, for at least some patients treated at that centre, early in the pandemic. The use of radical hypofractionated radiotherapy courses in this context did have some randomised controlled trial (RCT) data to support it [18]. However, responses from centres infer that decision-making was also pragmatic, weighing up possible reductions in efficacy by implementing such regimes, with the risks of not reducing acute toxicity, footfall, and overall treatment as the pandemic

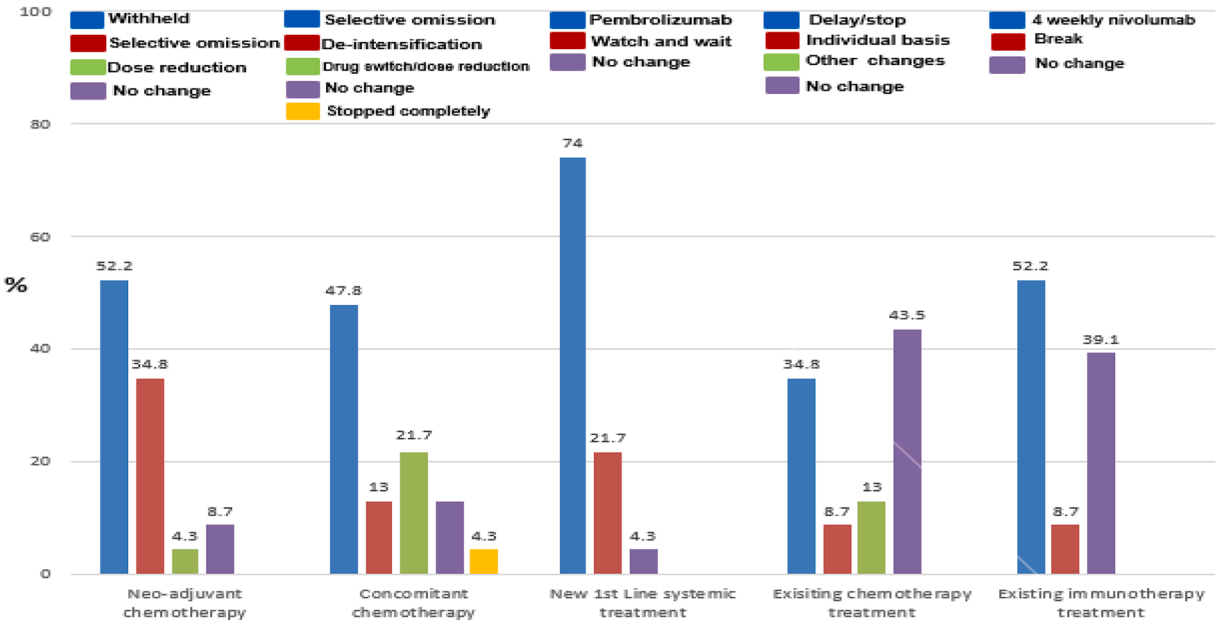

Fig. 3a. Systemic treatment changes during the first wave of COVID-9 pandemic; one centre included both selective omission for older patients and drug switch for younger patients (included in drug switch); The other centre included both selective omission and drug switch (included in drug switch).

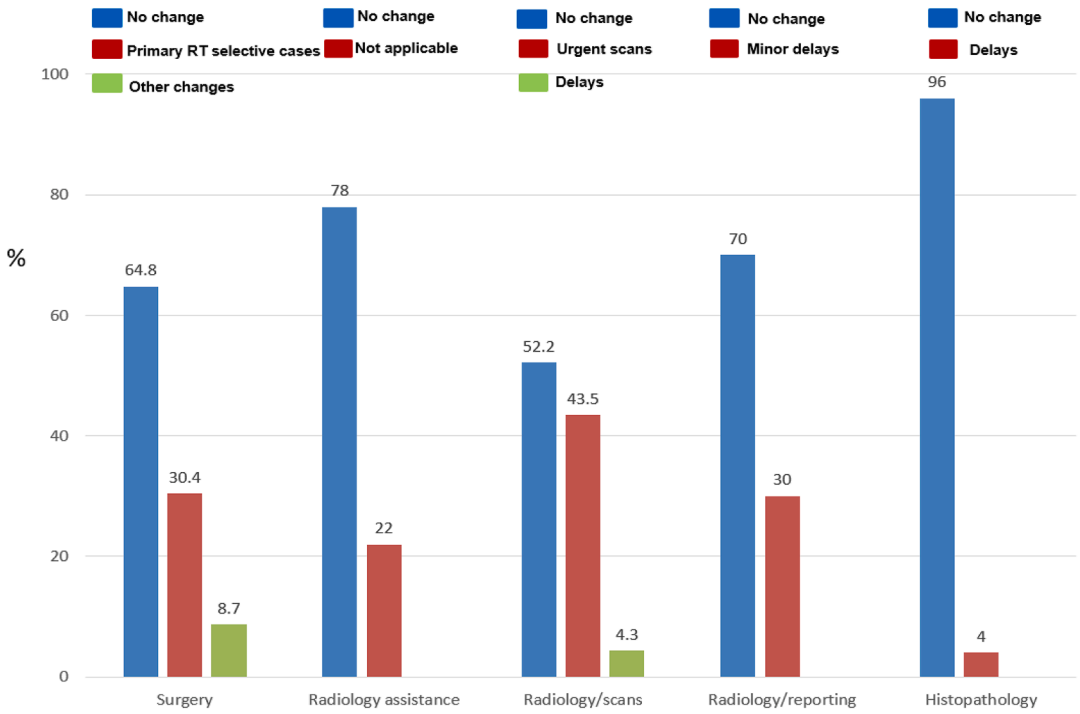

Fig. 3b. Changes in surgery, radiology assistance (input for radiotherapy contouring), radiology scans, radiology reporting and histopathology during the first wave of COVID-19 pandemic.

approached its zenith. It is worth stating that amongst individual centres having their own heterogenous challenges, national guidance from the Royal College of Radiologists (Clinical Oncology) was strongly advocating consideration of hypofractionation to reduce footfall and risk of infection [21].

This theme of there being broad alignment in the use of first principles to guide decision making, with more superficial heterogeneity in the application of these principles to daily practice, is also seen in our data on systemic therapy. In general, survival benefits with the addition of concomitant systemic therapy to radical radiotherapy in patients with HNC are modest [22]. Weighing against this, the addition of cisplatin chemotherapy to radical radiotherapy regimes, requires long infusion times in hospital, an increased risk of toxicity requiring emergency management, and some direct risks of immunosuppression, which was naturally a concern during the pandemic. Furthermore, the delivery of chemotherapy in some areas was compromised by staff availability, and even where this was less problematic the modest survival benefit had to be balanced against the short-term perceived risks related to the effects of COVID-19. The latter were clearly difficult to quantify, although groups at risk of severe COVID were identified early in the pandemic

[23].

This balance of risks is reflected in the data pertaining to concomitant therapy, with 14/23 centres (60.9%) either omitting concomitant therapy altogether, or in selected cases. In addition, for centres where concomitant therapy was continued during the pandemic, many chose to reduce total dose, or dose density, or switch to a regime thought to be less immunosuppressive, or add GCSF, in an attempt to mitigate perceived risks. Interestingly, 2 centres either started or increased their use of the accelerated DAHANCA regimen, whilst reducing use of concomitant systemic therapy, on the basis that this protocol confers similar additional disease control benefits, and acute toxicity risks relative to the addition of systemic therapy to standard fractionation approaches, but without the immunosuppression [18].

The data in this study confirm our pre-conception that feeding tube practice is highly variable across UK centres. Again, this is not surprising, as evidence for one feeding tube policy being more efficacious is inconclusive; a review investigating different nutritional policies concluded that there was insufficient evidence to determine the optimal method of enteral feeding [24]. However, the data also show similar trends in the way issues around feeding tubes were managed during the pandemic. The fact that 15/23 (65.2%) of centres reported no change to practice suggests that clinicians were generally reluctant to amend this aspect of treatment protocols unless determined by necessity. Interestingly, 2 centres (8.7%) switched from reactive to elective feeding tube insertion in an attempt to reduce the risk of acute hospital admission during the pandemic, whilst five of 23 centres (21.7%) had to switch from elective feeding tubes to reactive NGT, due to reduced capacity and access to endoscopy. However, in our view, it is a testament to our colleagues across the multi-disciplinary team that this proportion was so low, given the extreme pressures on hospitals at the time

As seen with practice changes in both radiotherapy and systemic therapy, the range and magnitude of additional pressures seen in the early stages of the pandemic had an inevitable effect on surgical practice – notably the big reduction in access to ITU beds. However, recent evidence has highlighted the safety of head and neck surgical practice during the COVID-19 pandemic [25]. Interestingly, where surgery was omitted, radiotherapy and/or chemotherapy was considered as a substitute or a temporising measure, slightly in conflict with the logic of arguments detailed above. Furthermore, where surgery could and did take place, this triggered further debate in the use, and technical details, of post-operative radiotherapy. Some evidence supported the indications and doses for treatment and helped to quantify the benefits of chemotherapy in this setting [26,27].

Our results are consistent with ASTRO/ESTRO recommendations, which were published during the peak of the 1st wave of the pandemic in April 2020 [12]. First of all, there was a strong agreement to suggest hypofractionation radiation schedule in case of severely reduced radiation therapy capacity; however, these changes were implemented during the risk mitigation phase in a lot of centres (61% of centres offering hypofractionation schedule to all or selected patients). Moreover, there was a strong agreement to continue with the use of concurrent chemotherapy with numerous panellists stating they would consider changing to weekly cisplatin. However, it was recognised that the use should be restricted in patients with a higher risk of more serious SARS-COV-2 infection such as patients with co-morbidities or of older age. This is also evident on the results of the survey with only one centre (4.3%) omitting chemotherapy for all patients and thirteen (56.5%) omitting in selected cases deemed as high-risk of infection and mortality. This was in agreement with the national guidance from the Royal College of Radiologists (Clinical Oncology) [21], which advocated omission of concurrent chemotherapy in patients over 60 years old or in those with significant comorbidity. Finally, there was a strong agreement not to increase the use of prophylactic feeding tube. As highlighted above, there are underlying discrepancies on feeding tube practice across UK centres. During the first wave of COVID-19 pandemic, 14/23 (60.9%) centres were using prophylactic feeding tubes with 2 of those centres changing their policy from reactive to prophylactic during the first wave.

One focus of the UK NCRI Head and Neck Clinical Studies Group has been to consider whether the changes instituted due to the epidemic present an opportunity to answer clinical research questions. The interventions described were generally short term, and implemented quickly, and often simultaneously across the country (and indeed internationally). It is relatively easy to identify the patients affected because the time at which clinical decisions and treatments were made is clearly defined. However, as we have demonstrated, centres across the country took differing approaches, changing management in a heterogeneous manner depending on local oncological and epidemiological considerations, and for varying lengths of time. Data on short term outcomes such as toxicity is poorly collected and not standardised outside clinical trials. Collection of long-term outcomes such as recurrence, feeding tube dependency, other quality of life outcomes and even death is also poor, and national initiatives to improve data quality following the Data Audit for Head and Neck Oncology (DAHNO) have faltered. Thus, whilst the notion of learning as much as we can from the pandemic is both scientifically and ethically laudable, we suggest that the problems described will confer very significant methodological challenges for those seeking to do so.

So what can be learned from the experience in Head and Neck oncology during the pandemic of 2020? This study shows that whilst the details of crisis response across the nation were heterogeneous, there were clear trends in the principles and logic that clinicians applied to weigh the relevant risks, before clinical data or consensus expert opinion was available to help frame these decisions. Furthermore, the study also shows considerable variation in many aspects of practice prior to the onset of the pandemic. Whilst the fundamentals of treatment for HNSCC are similar across the country, there is a lack of baseline consensus on the detailed application of issues as diverse as prophylactic dental management, feeding tube placement, radiotherapy fractionation and chemotherapy drugs and doses. We aim to collect the treatment and survival outcome data on some of these affected patients who had treatment modifications, which may provide lessons to be learnt for future pandemics. Moreover, it will be interesting to assess outcomes and the effect of delays to diagnosis and treatment as the delays reported in this survey were subjective and we did not report actual metrics.

In summary therefore, these data present an interesting paradox. In one sense, it is reassuring that centres across the country applied such similar approaches to dealing with the ‘once in a generation’ crisis presented by COVID-19. However, the crisis has also exposed underlying discrepancies in standard practice, and may provide an impetus to change. A timely initiative from the Royal College of Radiologists seeks to form a consensus on UK head and neck cancer management, as has been achieved in other tumour sites [28].

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Informed consent statement

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Data availability statement

All data relevant to the study are included in the article.

CRediT authorship contribution statement

Ifigenia Vasiliadou: Methodology, Formal analysis, Data curation, Writing – original draft. **David Noble:** Methodology, Formal analysis, Data curation, Writing – original draft. **Andrew Hartley:** Data curation. **Rafael Moleron:** Data curation. **Paul Sanghera:** Data curation. **Teresa**

Guerrero Urbano: Data curation. **Stefano Schipani:** Data curation. **Dorothy Gujral:** Data curation. **Bernie Foran:** Data curation. **Shree Bhide:** Data curation. **Anoop Haridass:** Data curation. **Kannon Nathan:** Data curation. **Andriana Michaelidou:** Data curation. **Mehmet Sen:** Data curation. **Konstantinos Geropantas:** Data curation. **Mano Joseph:** Data curation. **Lorcan O'Toole:** Data curation. **Matthew Griffin:** Data curation. **Laura Pettit:** Data curation. **Jonathan Chambers:** Data curation. **Petra Jankowska:** Data curation. **Emma De Winton:** Data curation. **Rebecca Goranova:** Data curation. **Niveditha Singh:** Data curation. **Ketan Shah:** Methodology, Formal analysis, Data curation, Writing – original draft, Writing - review & editing. **Anthony Kong Conceptualisation:** Methodology, Formal analysis, Resources, Data curation, Writing – original draft, Writing - review & editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ctro.2021.06.002.

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