Disease trajectories, place and mode of death in people with head and neck cancer: Findings from the 'Head and Neck 5000' population-based prospective clinical cohort study

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Abstract

Background: Few large studies describe initial disease trajectories and subsequent mortality in people with head and neck cancer. This is a necessary first step to identify the need for palliative care and associated services.
Aim: To analyse data from the Head and Neck 5000 study to present mortality, place and mode of death within 12 months of diagnosis.
Design: Prospective cohort study.
Participants: In total, 5402 people with a new diagnosis of head and neck cancer were recruited from 76 cancer centres in the United Kingdom between April 2011 and December 2014.
Results: Initially, 161/5402 (3%) and 5241/5402 (97%) of participants were treated with 'non-curative' and 'curative' intent, respectively. Within 12 months, 109/161 (68%) in the 'non-curative' group died compared with 482/5241 (9%) in the 'curative' group. Catastrophic bleed was the terminal event for 10.4% and 9.8% of people in 'non-curative' and 'curative' groups, respectively; terminal airway obstruction was recorded for 7.5% and 6.3% of people in the same corresponding groups. Similar proportions of people in both groups died in a hospice (22.9% 'non-curative'; 23.5% 'curative') and 45.7% of the 'curative' group died in hospital.
Conclusion: In addition to those with incurable head and neck cancer, there is a small but significant 'curative' subgroup of people who may have palliative needs shortly following diagnosis. Given the high mortality, risk of acute catastrophic event and frequent hospital death, clarifying the level and timing of palliative care services engagement would help provide assurance as to whether palliative care needs are being met.

Keywords

Head and neck cancer, mortality, palliative care, cohort studies

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What is already known about the topic?

- People with head and neck cancer have unique and complex needs due to the impact from both the disease and its treatment.
- Early engagement of Specialist Palliative Care has been shown to have a beneficial impact on cancer patients and family carers, but the best way to integrate this care for those with head and neck cancer needs further clarification.

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What this paper adds?

- Two-thirds of people with head and neck cancer treated with 'non-curative' intent and almost 10% of those treated with 'curative intent' died within the 12 months following initial diagnosis.
- Over a fifth of people with head and neck cancer, irrespective of their original treatment intent, died in a hospice which is greater than the proportion of those with cancer as a whole.
- Between 6% and 11% died from acute bleeding or airway obstruction.

Implications for practice, theory or policy

- Further understanding about current levels and timing of palliative care service engagement would be a useful next step in determining to what degree palliative care needs for those with head and neck cancer are met.
- Identifying people with 'high risk' head and neck cancer at the point of diagnosis and exploring their care needs in greater detail also represent an area of further study.

Background

Evidence to support the benefits of early access to Specialist Palliative Care, often concurrent with active oncology care, has expanded rapidly over the last decade. Studies suggest that Specialist Palliative Care improves quality of life, symptom control and aspects of doctor–patient communication.[1–6] There are a number of unanswered questions, however, relating to the optimum service model and how to promote timely patient identification and referral.[1] Previous studies have mainly focused on solid organ tumours such as lung and upper gastrointestinal cancer. Little attention has been paid to people with head and neck cancer despite the well-recognised complexities of both the cancer and its treatment.[7] Fundamental changes can occur affecting individuals' appearance[8,9] and their ability to eat, speak and breathe.[10–12] The subsequent psychological and social impact for both those with head and neck cancer and their family carers is significant.[13]

At presentation, about 60% of people with head and neck cancer have advanced disease (stage III or IV) and recurrence following treatment is high.[14,15] The median overall survival for those with recurrent or metastatic disease is less than 1 year.[16] Engagement with Specialist Palliative Care services can vary. One American study observed that individuals having a diagnosis of head and neck cancer was associated with early referral to 'Supportive and palliative care' services.[17] Another study involving those with terminal head and neck cancer (defined as having distal metastatic disease), however, suggested under-utilisation of in-patient palliative care consultations.[18] In order to develop and direct targeted services to best support people with head and neck cancer, a greater understanding of the potential palliative care needs and challenges for this population is required.[19] There are few large-scale studies describing initial disease trajectories and subsequent mortality of people with head and neck cancer – a necessary first step in identifying the potential need for palliative care.

We present results from the 'Head and Neck 5000' resource,[20,21] a large clinical cohort study in people with head and neck cancer within the United Kingdom. We focus on disease trajectories; compare mortality for those treated with 'non-curative' and 'curative' intent; examine the place and mode of death for those who died within the first 12 months; and assess the subsequent mortality during the study period.

Methods

Study population

The study methods have previously been described.[20] Within 76 UK cancer centres, all people aged 16 years or over with a new diagnosis of head and neck cancer were eligible. People treated with curative intent were recruited before treatment started (unless part of a diagnostic procedure) and participants offered palliative support were recruited as soon after diagnosis as possible.[22]

Recruitment

Participants were recruited between 1 April 2011 and 31 December 2014. Written informed consent, obtained by research nurses based in local centres, included consent for collection of clinical data from case records and record linkage.

Treatment intent

Baseline data capture forms completed by the research sites were used to define 'cancer plan intent',[21] defined as the intention of treatment, as specified in the final pre-treatment multi-disciplinary team (MDT) meeting. The research teams at each site were subsequently (4 months later) asked to indicate which option best reflected the treatment received (rather than planned) and were defined as:

- Curative: underwent treatment that intends, however slight the chance of success, to cure.
- Palliative anti-cancer: underwent treatments such as chemotherapy, radiotherapy or surgery but it is known that the cancer cannot be cured.
- Supportive: refers to 'best supportive care' aimed at relieving symptoms but is not as intensive a treatment as 'palliative anti-cancer'; it is known that the cancer cannot be cured.
- No specific anti-cancer: patient declined to have any treatment.

Within this study, participants were categorised into two groups reflecting the treatment they received – those treated with 'curative' intent and those treated with 'non-curative intent' (i.e. a combination of the other groups).

Baseline data collection

Health, lifestyle and socio-demographic measurements. Socio-demographic, health and lifestyle measures including age at consent, gender, smoking status, alcohol consumption and World Health Organization (WHO) performance status were collected using self-report questionnaires.[20] Smoking status was categorised as never, current or former smoker. Alcohol consumption was categorised as non-drinker, moderate drinker (<14 units per week for men and women), hazardous drinker (14–50 units/week for men and 14–35 units/week for women) and harmful drinker (>50 units/week for men and >35 units/week for women), where one unit of alcohol = 8 g/10 mL ethanol.[23] WHO performance status ranged from zero ('normal activity') to four ('confined to bed or chair more than 50 percent of the time').[24] We linked the English Index of Multiple Deprivation (IMD) 2010 quintiles using participants' home postcode – group 1 represented the most deprived people and group 5 represented the least deprived people.[25]

Clinical measures. Anatomical site was recorded using the International Classification of Diseases (ICD) 10 codes.[26] Where possible, clinical data were checked against pathology forms. We grouped anatomical site into: lip and oral cavity squamous cell carcinoma (SCC) (C00, C02-C06), oropharynx SCC (C01, C05.1, 2, C09.0, 1, 9, C10.0, 2, 3), larynx SCC (C32.0, 1, 2, C10.1), other SCC (C07-C08, C11-C14, C30-C31, C41.1, C69.5) and other non-SCC (and ICD code with non-SCC histology) tumours.

Other clinical data included clinical stage, co-morbidity status, treatment modality and human papillomavirus (HPV) status. Stage was grouped into four categories (I, II, III, IV) using the Tumour, Node and Metastasis version 7.[27] Comorbidity was measured using the Adult Comorbidity Evaluation[28] – participants were grouped into four categories including no co-morbidity, mild co-morbidity, moderate decompensation and severe decompensation. Treatment was defined at 4 months based on the treatment received (rather than planned). Anti-cancer treatments were defined as single modality (subdivided into 'surgery only', 'radiotherapy only' or 'chemotherapy only'); chemoradiotherapy only; surgery combined with other anti-cancer treatment; and no anti-cancer treatment. HPV status was defined as a serological response to HPV 16 E6 protein using a glutathione S-transferase multiplex assay undertaken at the German Cancer Research Center (DKFZ), Heidelberg, Germany. A cut-off value of more than 1000 median fluorescence intensity (MFI) units defined a positive response.[29,30]

Follow-up

Follow-up questionnaires were sent out 4 and 12 months after the participant was recruited and research nurses collected updated clinical information from hospital medical records concurrently. On 11 October 2018, the cohort was linked to the National Office of Statistics mortality data, which provided at least 3½ years of follow-up.

Statistical analysis

Demographic data are presented along with *p*-values to test for differences between 'curative' and 'non-curative' groups. Survival time was measured as the time from study consent until either death or the end of the most recent follow-up period. Cox proportional Hazards models were estimated with 95% confidence intervals (CIs) to determine differences in the predictors of all-cause mortality for each variable included in the analysis (both unadjusted and adjusted for age and sex) and to compare between 'curative' versus 'non-curative' models. *p*-values were displayed to test for the trend across each group for ordinal variables, and individual *p*-values were displayed to test for the differences between hazard ratios (HRs) for unordered variables. Descriptive data from mortality forms were presented along with percentages and 95% CI for proportions. All statistical analyses were performed using Stata (Version 15.0).[31,32]

Ethical approval

The study was approved by the National Research Ethics Committee (South West Frenchay Ethics Committee, reference 10/H0107/57, 5 November 2010) and approved by the research and development departments for participating NHS Trusts.

Results

Study population

From the 5511 participants who consented, 109 were excluded from analyses (Figure 1). From the remaining 5402, 161 (3%) were treated with 'non-curative' intent
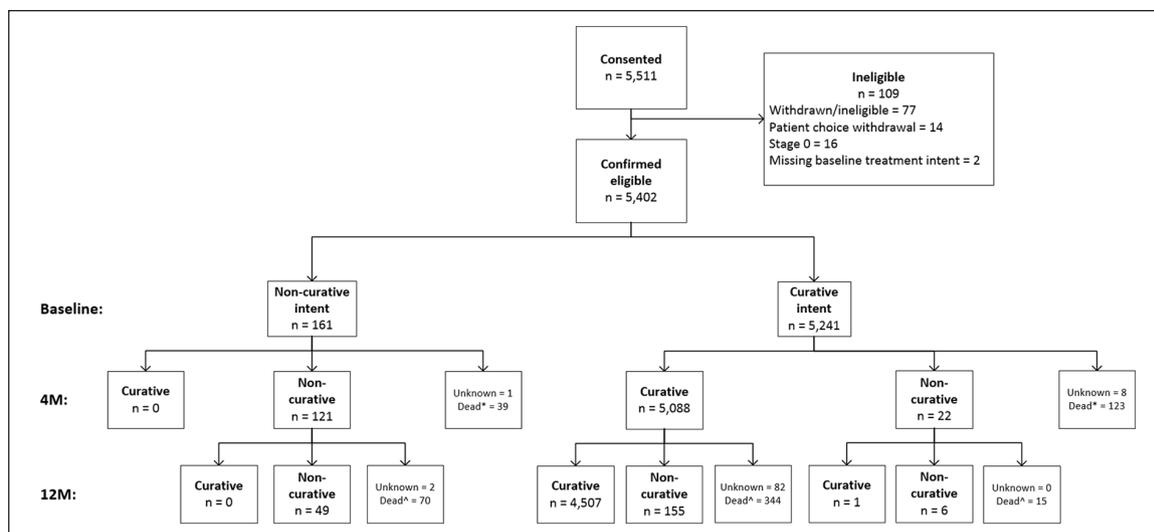
Figure 1. Diagram displaying cohort recruitment and status of patients receiving curative or non-curative treatment at baseline, 4 months and 12 months.
*Died between baseline and 4 months.
^Died between 4 and 12 months.
'Unknown' = patients are alive, but their treatment intent has not been recorded.

and 5241 (97%) treated with 'curative' intent. Comparison of baseline data between those treated with 'non-curative' and 'curative' intent showed those within the 'non-curative' group were older, had a higher proportion of moderate or severe co-morbidities, poorer WHO performance status and were twice as likely to present with Stage IV disease (Table 1). In addition, those within the 'non-curative' group were more likely to have 'other SCC' as their primary tumour site, be HPV-negative, not undergo surgery but rather have single or no definitive anti-cancer treatment.

Mortality up to 12 months following diagnosis

Within the first 4 months, 39/161 (24%) of those treated with 'non-curative' intent had died compared with 123/5241 (2.3%) of those in the 'curative' group. At 12 months, 109/161 (67.7%) of those in the 'non-curative' group had died. From the initial 'curative' intent group, 482/5241 (9%) had died and 162/5241 (3%) were now being treated with 'non-curative' intent (Figure 1). In total, 591/5402 (10.9%) had died within the initial 12 months following diagnosis.

Overall survival results

Participants were followed up for at least 3½ years. During this time, most people treated at baseline with 'non-curative' intent died (n = 147/161, 91.3%) as did 30% of those treated curatively (n = 1573/5241).

People in the 'non-curative' group had markedly worse survival than those with stage IV tumours in the 'curative' group (Figure 2). Within the 'non-curative' group, those with a poorer WHO performance status were more likely to die within the total study period (Table 2). Within the 'curative' group, those who were older, male, had severe co-morbidities, poor WHO performance status, a higher deprivation score, were currently smoking and with more advanced disease stage were more likely to die within the study period (Table 3). Those who were treated solely with chemotherapy had a markedly higher HR. There were only 14 people in this group, however, and nine were identified as 'non-curative' within 12 months.

People in the 'non-curative' group had a ninefold higher risk of death (unadjusted HR = 9.22 (95% CI, 7.8 to 11.0)) compared with those in the 'curative' group (Supplementary Table 1). Following full adjustment, the HR attenuated but they still had almost a threefold higher risk of all-cause mortality than the patients in the 'non-curative' group (HR = 2.95 (95% CI = 2.0 to 4.3).

Cause, mode and place of death

Mortality feedback forms were completed for 549/591 (93%) participants who died within the first year of the study (Table 4). From those in the 'non-curative' group, 5/48 (10.4%) people who had died within the first 12 months had a catastrophic bleed and 3/40 (7.5%) had an airway obstruction as a terminal event. Similarly, 22/224 (9.8%) and 12/192 (6.3%) from those in the 'curative' group had a bleed or airway obstruction, respectively.

Table 1. Comparison at baseline between 'non-curative' intent group and 'curative' intent group.

	Non-curative intent	Curative intent	*p*-value for trend
Total	161	5241	
Mean age at consent (SD)	69.1 (11.6)	60.6 (11.7)	<0.001
Age at consent group			
Less than 54	13 (8.1%)	1501 (28.6%)	<0.001
55–64	46 (28.6%)	1754 (33.5%)	
65 and older	102 (63.4%)	1986 (37.9%)	
Total	161	5242	
Gender			0.850
Male	116 (72.0%)	3812 (72.7%)	
Female	45 (28.0%)	1429 (27.3%)	
Total	161	5242	
Comorbidity			
No comorbidity	27 (16.9%)	2268 (44.3%)	<0.001
Mild	47 (29.4%)	1734 (33.8%)	
Moderate	50 (31.3%)	903 (17.6%)	
Severe decompensation	36 (22.5%)	219 (4.3%)	
Total	160	5125	
WHO performance status			
Normal activity	19 (20.0%)	2131 (56.7%)	<0.001
Strenuous activity restricted	31 (32.6%)	962 (25.6%)	
Up and about >50%	25 (26.3%)	504 (13.4%)	
Confined to bed or chair >50%	20 (21.1%)	163 (4.3%)	
Total	95	3759	
Smoking status			
Current smoker	25 (25.8%)	722 (19.4%)	0.064
Former smoker	57 (58.8%)	2081 (55.8%)	
Never smoked	15 (15.5%)	926 (24.8%)	
Total	97	3728	
Alcohol			
Non-drinker	32 (33.0%)	1075 (28.3%)	0.410
Moderate drinker	17 (17.5%)	856 (22.5%)	
Hazardous/harmful drinker	48 (49.5%)	1873 (49.2%)	
Total	97	3733	
IMD Quintile[a]			
1 – Most deprived	39 (27.7%)	1006 (21.0%)	0.081
2	34 (24.1%)	914 (19.1%)	
3	22 (15.6%)	1056 (22.0%)	
4	23 (16.3%)	903 (18.8%)	
5 – Most affluent	23 (16.3%)	916 (19.1%)	
Total	141	4794	
Tumour site			
Oral cavity SCC	28 (17.7%)	1247 (23.9%)	<0.001
Oropharynx SCC	37 (23.4%)	1848 (35.4%)	
Larynx SCC	22 (13.9%)	1019 (19.5%)	
Other SCC	53 (33.5%)	575 (11.0%)	
Non-SCC	18 (11.4%)	535 (10.2%)	
Total	158	5225	
Tumour stage			
I/II/III	22 (15.4%)	2766 (55.2%)	<0.001
IV	121 (84.6%)	2245 (44.8%)	
Total	143	5009	
HPV-16 Status			
Negative	118 (92.2%)	3154 (71.5%)	<0.001
Positive	10 (7.8%)	1257 (28.5%)	

(Continued)

Table 1. (Continued)

	Non-curative intent	Curative intent	*p*-value for trend
Total	128	4418	
Treatment			<0.001
Surgery only	3 (1.9%)	1311 (25.0%)	
Chemoradiotherapy only	21 (13.0%)	1563 (29.8%)	
Radiotherapy only	81 (50.3%)	970 (18.5%)	
Surgery and radio/chemo/chemoradio	4 (2.5%)	1359 (25.9%)	
Chemotherapy only	21 (13.0%)	14 (0.3%)	
No anti-cancer treatment	31 (19.3%)	24 (0.5%)	
Total	161	5242	

WHO: World Health Organization; IMD: English Index of Multiple Deprivation; SCC: squamous cell carcinoma; HPV: human papillomavirus; SD: standard deviation.
[a]English patients only.
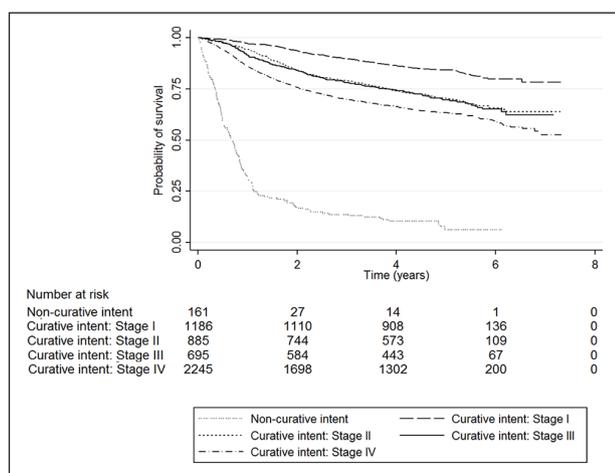
Figure 2. Kaplan–Meier plot of survival up to 8 years after diagnosis comparing non-curative with curative treatment intent (curative intent stratified by stage).

From those who had died within the first 12 months and had a completed mortality form, there was a suggestion that more of those in the 'curative' group died in hospital compared with the 'non-curative' group (*p* = 0.09) (Table 4). Similar proportions of those within the 'non-curative' (23.5%) and 'curative' (22.9%) groups died in a hospice.

Discussion

Main findings

The vast majority of people within this cohort were treated with curative intent. The small proportion treated with 'non-curative' intent had recognised risk factors that were associated with poor prognosis including increasing age, advanced stage of disease and multiple co-morbidities. Two-thirds of those initially treated with 'non-curative' intent and almost 10% of those treated curatively died within the first 12 months following initial head and neck cancer diagnosis. The latter group potentially represents a cohort of people who after undergoing initial curative treatment were quickly identified to have residual or recurrent cancer, necessitating a change in treatment intent to a palliative approach.

During the study period, the risk of death was over nine times greater for those in the 'non-curative' group compared with the 'curative' group. From the participants who died within 12 months of diagnosis, over one-fifth of people with head and neck cancer, irrespective of their original treatment intent, died in a hospice.

What this study adds and implications for practice

When an individual is diagnosed with head and neck cancer, survival and treatments that offer the best chance of cure are usually the primary concern.[33] Hence, it is unsurprising that most people in our study were treated with 'curative' intent at the point of diagnosis. Knowledge about place of death helps our understanding regarding service needs and development. From those who died within the first 12 months, over a fifth of people with head and neck cancer, irrespective of their original treatment intent, died in a hospice. This is greater than the observed numbers of head and neck cancer deaths in a 'hospice ward' (14.6%) within a large Taiwanese study.[34] The observed proportion of hospice deaths is also greater than the 16% of people with all forms of cancer who died within a hospice in England between 1993 and 2010.[35] In part, this may reflect the complexities of care, including the risk of acute catastrophic events and the need for specialist care. Within this cohort, between 6% and 11% had a catastrophic event as a terminal event, greater than the 3%–5% previously reported to have 'carotid blowout syndrome'.[36]

Different models of providing palliative care exist,[37] but the optimum model for those with head and neck cancer remains unclear. Compared with other cancers,

Table 2. Predictors of survival in people treated with non-curative intent at baseline.

	Unadjusted model	*p*-value	Age- and sex-adjusted model	*p*-value
Age at consent group (*n* = 161)		0.793*		
Less than 54	1.00 (Ref.)		–	–
55 to 64	0.75 (0.40, 1.40)		–	–
65 and older	0.81 (0.45, 1.45)		–	–
Gender (*n* = 161)		0.843		
Male	0.96 (0.67, 1.38)		–	–
Female	1.00 (Ref.)		–	–
Comorbidity (*n* = 160)		0.484*		0.379*
No comorbidity	1.00 (Ref.)		1.00 (Ref.)	
Mild	1.21 (0.74, 2.00)		1.36 (0.78, 2.34)	
Moderate	1.20 (0.74, 1.96)		1.33 (0.78, 2.25)	
Severe decompensation	1.24 (0.73, 2.09)		1.35 (0.78, 2.34)	
WHO performance status (*n* = 95)		0.069*		0.016*
Normal activity	1.00 (Ref.)		1.00 (Ref.)	
Strenuous activity restricted	0.90 (0.49, 1.66)		0.84 (0.43, 1.62)	
Up and about >50%	1.13 (0.61, 2.12)		1.16 (0.59, 2.29)	
Confined to bed or chair >50%	1.77 (0.92, 3.39)		2.27 (1.14, 4.54)	
Smoking status (*n* = 97)		0.577*		0.817*
Current smoker	0.90 (0.45, 1.80)		0.94 (0.45, 1.95)	
Former smoker	1.29 (0.70, 2.37)		1.22 (0.66, 2.29)	
Never smoked	1.00 (Ref.)		1.00 (Ref.)	
Alcohol consumption (*n* = 97)		0.461*		0.735*
Non-drinker	1.00 (Ref.)		1.00 (Ref.)	
Moderate drinker	0.63 (0.33, 1.21)		0.63 (0.33, 1.21)	
Hazardous/harmful drinker	0.81 (0.50, 1.30)		0.90 (0.56, 1.47)	
IMD Quintile (*n* = 141)		0.706*		0.728*
1 – Most deprived	1.00 (0.59, 1.72)		1.01 (0.59, 1.73)	
2	0.81 (0.47, 1.39)		0.78 (0.45, 1.36)	
3	0.60 (0.33, 1.12)		0.60 (0.32, 1.11)	
4	0.76 (0.41, 1.40)		0.75 (0.40, 1.41)	
5 – Most affluent	1.00 (Ref.)		1.00 (Ref.)	
Tumour site (*n* = 158)				
Oral cavity SCC	1.00 (Ref.)		1.00 (Ref.)	
Oropharynx SCC	0.82 (0.49, 1.37)	0.438	0.78 (0.45, 1.34)	0.359
Larynx SCC	0.76 (0.42, 1.37)	0.364	0.76 (0.42, 1.36)	0.365
Other SCC	0.82 (0.51, 1.31)	0.399	0.81 (0.50, 1.33)	0.411
Non-SCC	0.61 (0.32, 1.16)	0.133	0.61 (0.32, 1.15)	0.125
Tumour stage (*n* = 143)		0.332		0.416
I/II/III	1.00 (Ref.)		1.00 (Ref.)	
IV	1.27 (0.78, 2.07)		1.23 (0.75, 2.03)	
HPV-16 Status (*n* = 123)		0.884		0.854
Negative	1.00 (Ref.)		1.00 (Ref.)	
Positive	1.05 (0.53, 2.08)		1.07 (0.51, 2.28)	
Treatment (*n* = 161)				
Surgery only	1.00 (Ref.)		1.00 (Ref.)	
Chemoradiotherapy only	0.98 (0.29, 3.31)	0.970	0.96 (0.27, 3.36)	0.945
Radiotherapy only	1.07 (0.34, 3.40)	0.912	1.10 (0.34, 3.51)	0.873
Surgery and radio/chemo/chemoradio	0.47 (0.09, 2.32)	0.353	0.47 (0.09, 2.36)	0.361
Chemotherapy only	0.86 (0.25, 2.92)	0.809	0.87 (0.25, 3.03)	0.831
No anti-cancer treatment	1.97 (0.60, 6.51)	0.264	2.08 (0.62, 6.96)	0.236

WHO: World Health Organization; IMD: English Index of Multiple Deprivation; SCC: squamous cell carcinoma; HPV: human papillomavirus.
p-value for trend.

Table 3. Predictors of survival in people treated with curative intent at baseline.

	Unadjusted model	HR *p*-value	Age- and sex-adjusted model	HR *p*-value
Age at consent group (*n* = 5241)		<0.001*		
Less than 54	1.00 (Ref.)		–	–
55 to 64	1.60 (1.38, 1.85)		–	–
65 and older	2.35 (2.05, 2.69)		–	–
Gender (*n* = 5241)		<0.001*		
Male	1.46 (1.29, 1.65)		–	–
Female	1.00 (Ref.)		–	–
Comorbidity (*n* = 5214)		<0.001*		<0.001*
No comorbidity	1.00 (Ref.)		1.00 (Ref.)	
Mild	1.66 (1.47, 1.88)		1.43 (1.27, 1.63)	
Moderate	2.53 (2.21, 2.89)		2.11 (1.84, 2.43)	
Severe decompensation	4.30 (3.56, 5.21)		3.51 (2.88, 4.27)	
WHO performance status (*n* = 3760)		<0.001*		<0.001*
Normal activity	1.00 (Ref.)		1.00 (Ref.)	
Strenuous activity restricted	1.88 (1.63, 2.18)		1.79 (1.55, 2.08)	
Up and about >50%	2.46 (2.08, 2.91)		2.33 (1.97, 2.76)	
Confined to bed or chair >50%	3.90 (3.11, 4.89)		3.60 (2.87, 4.51)	
Smoking status (*n* = 3729)		<0.001*		<0.001*
Current smoker	2.84 (2.34, 3.43)		2.83 (2.34, 3.44)	
Former smoker	1.73 (1.45, 2.06)		1.57 (1.32, 1.87)	
Never smoked	1.00 (Ref.)		1.00 (Ref.)	
Alcohol consumption (*n* = 3804)		0.203*		0.404*
Non-drinker	1.00 (Ref.)		1.00 (Ref.)	
Moderate drinker	0.74 (0.61, 0.88)		0.71 (0.59, 0.86)	
Hazardous/harmful drinker	1.05 (0.91, 1.21)		1.02 (0.88, 1.18)	
IMD Quintile (*n* = 4795)		<0.001*		<0.001*
1 – Most deprived	1.43 (1.21, 1.68)		1.49 (1.27, 1.76)	
2	1.25 (1.05, 1.48)		1.27 (1.08, 1.51)	
3	1.16 (0.98, 1.38)		1.17 (0.99, 1.38)	
4	0.98 (0.82, 1.18)		0.97 (0.81, 1.16)	
5 – Most affluent	1.00 (Ref.)		1.00 (Ref.)	
Tumour site (*n* = 5224)				
Oral cavity SCC	1.00 (Ref.)		1.00 (Ref.)	
Oropharynx SCC	0.70 (0.62, 0.80)	<0.001	0.73 (0.64, 0.83)	<0.001
Larynx SCC	0.81 (0.70, 0.93)	0.004	0.68 (0.58, 0.79)	<0.001
Other SCC	1.13 (0.96, 1.32)	0.146	1.13 (0.96, 1.32)	0.152
Non-SCC	0.46 (0.37, 0.58)	<0.001	0.57 (0.45, 0.71)	<0.001
Tumour stage (*n* = 5011)		<0.001		<0.001
I/II/III	1.00 (Ref.)		1.00 (Ref.)	
IV	1.74 (1.57, 1.93)		1.82 (1.64, 2.02)	
HPV-16 Status (*n* = 4411)		<0.001		<0.001
Negative	1.00 (Ref.)		1.00 (Ref.)	
Positive	0.47 (0.41, 0.55)		0.50 (0.44, 0.58)	
Treatment (*n* = 5241)				
Surgery only	1.00 (Ref.)		1.00 (Ref.)	
Chemoradiotherapy only	1.58 (1.36, 1.84)	<0.001	1.65 (1.41, 1.92)	<0.001
Radiotherapy only	2.02 (1.72, 2.37)	<0.001	1.67 (1.41, 1.96)	<0.001
Surgery and radio/chemo/chemoradio	1.94 (1.66, 2.25)	<0.001	1.94 (1.67, 2.26)	<0.001
Chemotherapy only	27.10 (15.49, 47.39)	<0.001	26.47 (15.11, 46.37)	<0.001
No anti-cancer treatment	6.97 (4.20, 11.55)	<0.001	6.84 (4.12, 11.34)	<0.001

HR: hazard ratio; WHO: World Health Organization; IMD: English Index of Multiple Deprivation; SCC: squamous cell carcinoma; HPV: human papillomavirus.
p-value for trend.

Table 4. Details from mortality feedback forms returned 1-year after diagnosis.

	Non-curative intent	% (95% CIs)	Curative intent	% (95% CIs)	*p*-value
Total deaths within 1 year of follow-up	109	–	482	–	–
Total mortality forms	103	–	446	–	–
Did this participant have a catastrophic bleed as a terminal event?					
Yes	5	10.4 (4.3, 23.3)	22	9.5 (6.3, 14.0)	0.84
No	43	89.6 (76.7, 95.7)	210	90.5 (86.0, 93.7)	
Total	48		224		
Did this participant have an airway obstruction as a terminal event?					
Yes	3	7.5 (2.3, 21.7)	12	6.1 (3.5, 10.4)	
No	37	92.5 (78.3, 97.7)	186	93.9 (89.6, 96.5)	
Total	40		192		
What was the place of death?					
Home	40	40.8 (31.3, 51.0)	114	28.6 (24.4, 33.3)	0.097
Hospice	23	23.5 (16.0, 33.0)	91	22.9 (19.0, 27.3)	
Hospital	31	31.6 (23.1, 41.6)	182	45.7 (40.9, 50.7)	
Care home	3	3.1 (1.0, 9.2)	8	2.0 (1.0, 4.0)	
Other	1	1.0 (0.1, 7.1)	3	0.8 (0.2, 2.3)	
Total	98		399		

CI: confidence interval.

people with head and neck cancer have a high prevalence of palliative care needs,[38] complex symptoms,[39] and frequently require opioids and other medications to help with symptom control.[40] Hence, developing and testing different models of care should be the focus of future studies. Within India, the first randomised controlled study assessing the impact of early Specialist Palliative Care with stage IV head and neck cancer patients is currently being conducted (Muckaden MA, personal communication). Specialist Palliative Care is a limited resource. Hence, it is important to identify patients who most need specialist input and those who may benefit from a broader palliative and supportive care approach provided by the wider MDT. From our study, there appear to be two groups where screening for unmet needs and linkage into specialist palliative care services may be required shortly after diagnosis: those initially treated with 'non-curative' intent and a 'high risk' subgroup of those initially treated with 'curative' intent, but who die within the first 12 months. Trying to prospectively identify this latter group remains a challenge.

To further understand the patient journeys, especially within the last year of life, undertaking research to explore the patient and family carer experience, symptom burden and the level of healthcare utilisation would be beneficial. As part of a German multi-centre prospective study, the symptoms and needs of head and neck cancer patients at the point of incurability are being assessed using self-reported tools.[41] An alternative method would be to undertake both longitudinal quantitative and qualitative research recruiting people with head and neck cancer and their families as they move from curative disease to palliative care. The addition of longitudinal qualitative methodology provides rich insights into an individual's changing experience of their illness.[42–44]

Knowing more about the factors influencing treatment decision-making, especially when the chance of cure is small, would also be beneficial. Within the United Kingdom, a previous study suggested only 25% of head and neck cancer multi-disciplinary meetings (forums used to discuss the diagnosis and treatment planning) have direct presence from Specialist Palliative Care[45] and it is unclear how much this situation has changed. A Dutch study examined the methods in which prognosis was communicated to people with head and neck cancer at various stages of their illness.[46] Specific prognostic information was often not included in these discussions and subsequent work is being conducted to help enhance shared decision-making.[46]

Finally, more detailed analysis of specific situations, using a 'confidential enquiry' approach, could help to better understand the circumstances of deaths leading up to an acute catastrophic event and identify ways that these could be predicted, prevented or better managed.

Strengths and limitations of the study

This study has several strengths. First, it is a large, prospective, national clinical cohort study which recruited people newly diagnosed with head and neck cancer. Second, those treated with 'non-curative' and 'curative' intent were recruited contemporaneously allowing comparisons between groups. Finally, the study collected prospective data on mortality and place of death.

The study had several weaknesses. First, the numbers within the 'non-curative' group were small. This limits the study's power and is reflected by the wide CIs for some analyses. Second, possible issues including perceived study burden and gatekeeping may have limited numbers of palliative participants who were recruited to the study. In addition, we do not have the reasons for non-participation, for example, lacks capacity and unwilling to complete study questionnaires. It is possible that those treated with palliative intent and subsequently recruited are not representative of all people treated with palliative intent.[47,48] In one study, 84/390 (21.5%) people with head and neck cancer were treated with palliative intent following diagnosis.[49] Third, the extent of missing data, especially for the place and mode of death, and the fact that data were recorded by the research team (rather than the clinical team) may limit their accuracy. More robust methods of eliciting this information would be useful within future research. Finally, the limited information available about the timing of referral and level of palliative care intervention leading up to death meant it was not possible to describe care pathways in detail.

Conclusion

In addition to those with incurable head and neck cancer, there is a small but significant 'curative' subgroup of people who may have palliative needs shortly following diagnosis. Given the high mortality, risk of acute catastrophic events and frequent hospital death, clarifying the level and timing of palliative care services engagement would help provide assurance as to whether palliative care needs are being met. Effective models of palliative care that provide timely support, potentially including access to Specialist Palliative Care teams at the time of treatment planning, are important to support both people with head and neck cancer and their family carers.

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Supplemental material

Supplemental material for this article is available online.

References

1. Hui D, Hannon BL, Zimmermann C, et al. Improving patient and caregiver outcomes in oncology: team-based, timely and targeted palliative care. *CA Cancer J Clin* 2018; 68(5): 356–376.
2. Temel J, Greer J, Muzikansky A, et al. Early palliative care for patients with metastatic non-small cell lung cancer. *N Eng J Med* 2010; 363(8): 733–742.
3. Bakitas MA, Tosteson TD, Li Z, et al. Early versus delayed initiation of concurrent palliative oncology care: patient outcomes in the ENABLE III randomised controlled trial. *J Clin Oncol* 2015; 33(13): 1438–1445.
4. Zimmermann C, Swami N, Krzyzanowska M, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *Lancet* 2014; 383(9930): 1721–1730.
5. Haun MW, Estel S, Rucker G, et al. Early palliative care for improving quality of life and survival time in adults with

advanced cancer: meta-analytical findings from a Cochrane review. *J Clin Oncol* 2016; 34(Suppl. 15): 10132.

6. Gaertner J, Siemens W, Meerpohl JJ, et al. Effect of specialist palliative care on quality of life in adults with advanced incurable illness in hospital, hospice, or community settings: a systematic review and meta-analysis. *BMJ* 2017; 357: j2925.

7. Mayland CR and Payne S. Head and neck cancer: a marginalised group? *Pall Med* 2018; 32(8): 1286–1287.

8. Callahan C. Facial disfigurement and sense of self in head and neck cancer. *Soc Work Health Care* 2004; 40(2): 73–87.

9. Henry M, Ho A, Lambert SD, et al. Looking beyond disfigurement: the experience of patients with head and neck cancer. *J Palliat Care* 2014; 30(1): 5–15.

10. Lokker ME, Offerman MP, van der Velden LA, et al. Symptoms of patients with incurable head and neck cancer: prevalence and impact on daily functioning. *Head Neck* 2013; 35(6): 868–876.

11. National Institute of Clinical Excellence (NICE). *Guidance on cancer services. Improving outcomes in head and neck cancer. The manual*. London: NICE, 2004.

12. Ferlito A, Rogers SN, Shaha AR, et al. Quality of life in head and neck cancer. *Acta Otolaryngol* 2003; 123: 5–7.

13. Shuman AG, Yang Y, Taylor JMG, et al. End-of-life care among head and neck cancer patients. *Otolaryng Head Neck* 2010; 144: 733–739.

14. Schenker Y, Robert MA, Bauman JE, et al. An enhanced role for palliative care in multidisciplinary approach for high risk head and neck cancer. *Cancer* 2016; 122(3): 340–343.

15. Cancer Research UK. Head and neck cancer incidence by stage at diagnosis, https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/head-and-neck-cancers/incidence#heading-Three (accessed 5 June 2019).

16. Vermorken JB and Spencer P. Optimal treatment options for recurrent/metastatic head and neck cancer. *Ann Oncol* 2010; 21(Suppl. 7): vii252–vii261.

17. Kwon JH, Hui D, Chisholm G, et al. Clinical characteristics of cancer patients referred early to supportive and palliative care. *J Palliat Med* 2013; 16(2): 148–155.

18. Mulvey CL, Smith TJ and Gourin CG. Use of inpatient palliative care services in patients with metastatic incurable head and neck cancer. *Head Neck* 2016; 38(3): 355–363.

19. Temel JS, Greer JA, El-Jawahri A, et al. Effects of early integrated palliative care in patients with lung and GI cancer: a randomised clinical trial. *J Clin Oncology* 2017; 35(8): 834–841.

20. Ness AR, Waylen A, Hurley K, et al. Establishing a large prospective clinical cohort in people with head and neck cancer as a biomedical resource: head and neck 5000. *BMC Cancer* 2014; 14: 973–978.

21. University of Bristol and University Hospitals Bristol NHS Foundation Trust. Head and Neck 5000 – a research study of people with head and neck cancer, http://www.headandneck5000.org.uk (accessed 15 April 2019).

22. Ness AR, Waylen A, Hurley K, et al. Recruitment, response rates and characteristics of 5511 people enrolled in a prospective clinical cohort study: head and neck 5000. *Clin Otolaryngol* 2016; 41(6): 804–809.

23. National Institute for Health and Clinical Excellence. Alcohol-use disorders: prevention, June 2010, https://www.nice.org.uk/guidance/ph24/chapter/8-Glossary#alcohol-dependence (accessed 15 April 2019).

24. Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol* 1982; 5(6): 649–655.

25. McLennan D, Barnes H, Noble M, et al. The English Indices of Deprivation 2010. Department of Communities and Local Government 2011, https://www.gov.uk/government/statistics/english-indices-of-deprivation-2010 (accessed 11 September 2019).

26. WHO. ICD-10 Version: 2016, https://icd.who.int/browse10/2016/en (accessed 11 September 2019).

27. Sobin L, Gospodarowicz M and Wittekind C. *TNM classification of malignant tumours*, 7th ed. New York: Wiley-Blackwell, 2009.

28. Piccirillo JF and Feinstein AR. Clinical symptoms and co-morbidity: significance for the prognostic classification of cancer. *Cancer* 1996; 77(5): 834–842.

29. Waterboer T, Sehr P, Michael KM, et al. Multiplex human papillomavirus serology based on in situ–purified glutathione-S-transferase fusion proteins. *Clin Chem* 2005; 51(10): 1845–1853.

30. Schroeder L, Wichmann G, Willner M, et al. Antibodies against human papillomaviruses as diagnostic and prognostic biomarker in patients with neck squamous cell carcinoma from unknown primary. *Int J Cancer* 2017; 142: 1361–1368.

31. StataCorp LLC. *Stata statistical software: release 15*. College Station, TX: StataCorp LLC, 2017.

32. Rogers S, Semple C, Babb M, et al. 2016 quality of life considerations in head and neck cancer: United Kingdom National Multidisciplinary Guidelines. *J Laryngol Otol* 2016; 130(Suppl. S2): S49–S52.

33. Gill SS, Frew J, Fry A, et al. Priorities for the head and neck cancer patient, their companion and members of the multidisciplinary team and decision regret. *Clin Oncol* 2011; 23(8): 518–524.

34. Kuo TL, Lin CH, Jiang RS, et al. End-of-life care for head and neck cancer patients: a population-based study. *Support Care Cancer* 2017; 25(5): 1529–1536.

35. Gao W, Ho YK, Verne J, et al. Changing patterns in place of cancer death in England: a population-based study. *PLoS Med* 2013; 10(3): e1001410.

36. Powitzky R, Vasan N, Krempl G, et al. Carotid blowout in patients with head and neck cancer. *Ann Otol Rhinol Laryngol* 2010; 119: 476–484.

37. Brereton L, Clark J, Ingleton C, et al. What do we know about different models of providing palliative care? Findings from a systematic review of reviews. *Palliat Med* 2017; 31(9): 781–797.

38. Becker G, Hatami I, Xander C, et al. Palliative cancer care: an epidemiologic study. *J Clin Oncol* 2011; 29(6): 646–650.

39. Lal P, Verma M, Kumar G, et al. Initial experience of head and neck cancer patients treated in an oncologist led palliative care clinic at a tertiary cancer care centre in Uttar Pradesh: is the initiative of a full-fledged palliative care for cancer patients justified. *Indian J Palliat Care* 2016; 22(4): 477–484.

40. Heinonen T, Loimu V, Saarilahti K, et al. End-of-life care pathway of head and neck cancer patients: single-institution experience. *Eur Arch Otorhinolaryngol* 2018; 275(2): 545–551.

41. Alt-Epping B, Seidel W, Vogt J, et al. Symptoms and needs of head and neck cancer patients at diagnosis of incurability – Prevalences, clinical implications, and feasibility of a prospective longitudinal multicenter cohort study. *Oncol Res Treat* 2016; 39(4): 186–191.

42. Murray SA, Kendall M, Carduff E, et al. Use of serial qualitative interviews to understand patients' evolving experiences and needs. *BMJ* 2009; 339: b3702.

43. Carduff E, Murray SA and Kendall M. Methodological developments in qualitative longitudinal research: the advantages and challenges of regular telephone contact with participants in a qualitative longitudinal interview study. *BMC Res Notes* 2015; 8: 142.

44. Isaksson J, Salander P, Lilliehorn S, et al. Living an everyday life with head and neck cancer 2-2.5 years post-diagnosis – a qualitative prospective study of 56 patients. *Soc Sci Med* 2016; 154: 54–61.

45. Bradley PJ, Zutshi B and Nutting CM. An audit of clinical resources available for the care of head and neck cancer patients in England. *Clin Oncol* 2005; 17(8): 604–609.

46. Dronkers EAC, Hoesseini A, de Boer MF, et al. Communication of prognosis in head and neck cancer patients; a descriptive qualitative analysis. *Oral Oncol* 2018; 84: 76–81.

47. Timon C and Reilly K. Head and neck mucosal squamous cell carcinoma results of palliative management. *J Laryngol Otol* 2006; 120(5): 389–392.

48. Hughley BB, Sperry SM, Thomsen TA, et al. Survival outcomes in elderly patients with untreated upper aerodigestive tract cancer. *Head Neck* 2017; 39(2): 215–218.

49. Begbie FD, Douglas CM, Finlay F, et al. Palliative intent treatment for head and neck cancer: an analysis of practice and outcomes. *J Laryngol Otol* 2019; 133(4): 313–317.