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Estimation of an optimal chemotherapy utilisation rate for head and neck carcinoma: Setting an evidence-based benchmark for the best-quality cancer care

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ABSTRACT

Background: We estimated the optimal chemotherapy utilisation rate for head and neck cancer as a benchmark for measuring and improving the quality of cancer care.
Methods: An optimal chemotherapy utilisation tree was constructed using indications for chemotherapy that were identified from evidence-based treatment guidelines. Data on the proportion of patient and tumour-related attributes for which chemotherapy was indicated were obtained and merged with the treatment indications to calculate the optimal utilisation rate. The robustness of the model was tested with sensitivity analysis and Monte Carlo simulation. The optimal chemotherapy utilisation rate was compared with actual utilisation rates reported.
Results: Chemotherapy is indicated at least once in 36% (95% CI, 33–38%) of all patients with head and neck carcinoma. The optimal utilisation rates by subsites were as follows: lip, 8%; oral cavity, 40%; nasopharynx, 69%; oropharynx, 66%; hypopharynx, 74%; larynx, 43%; salivary gland, 48% and paranasal sinus with nasal cavity, 38%.
Conclusions: The optimal proportion of patients who should receive chemotherapy in the head and neck carcinoma population has risen significantly over the past 20 years. This temporal rise does not appear to be reflected in the limited actual utilisation rates that are available for comparison. Large population-based studies are recommended to further assess the current practice and compliance to guideline recommended care.

1. Introduction

Chemotherapy plays an integral role in the cure and palliation of patients with head and neck carcinoma. An estimate of the proportion of new cases of cancer who should receive chemotherapy at least once (optimal chemotherapy utilisation rate) is useful for planning and benchmarking chemotherapy services. Large population-based studies have reported that the actual chemotherapy utilisation rates in head and neck carcinoma varied from 12% to 17%.[1,2] A previously estimated benchmark for optimal radiotherapy utilisation in head and neck carcinoma has provided valuable insight into the shortfalls between ideal and current practice.[3] To our knowledge, the optimal chemotherapy utilisation rates in head and neck carcinoma are unknown, and no evidence-based benchmarks have been set as a measure for quality improvement in these patients. The objectives of this study were to estimate the proportion of patients with head and neck carcinoma who

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Table 1 – Head and Neck Cancer: Indications for Chemotherapy – Levels and sources of evidence.

Outcome No.	Clinical scenario	Treatment indicated	Level of evidence*	Ref.	Proportion of all head and neck cancer patients
3	Lip cancer, locoregional disease, distant recurrence following salvage treatment, good PS	Palliative CT	IV	NCCN.[5] NCI PDQ[6]	0.01
4	Lip cancer, locoregional disease, distant recurrence following local treatment, good PS	Palliative CT	IV	NCCN[5] NCI DQ[6]	0.01
5	Lip cancer, metastatic disease, good PS	Palliative CT	IV	NCCN[5] NCI PDQ[6]	0.01
7	Oral cavity cancer, stages I and II, recurrence, unsalvageable disease, good PS	Palliative CT	IV	NCCN.[5] NCI PDQ[6]	0.04
9	Oral cavity cancer, stages III and IV, suitable for surgery, extracapsular extension and/or positive margins, good PS	Post-op RT + CT	I	NCCN[5] NCI PDQ[6] CCO[23]	0.02
11	Oral cavity cancer, stages III and IV, suitable for surgery, no extracapsular nodal extension and/or positive margins, recurrence, unsalvageable disease, good PS	Palliative CT	IV	NCCN[5] NCI PDQ[6]	0.02
13	Oral cavity cancer, stages III and IV, unsuitable for surgery, good PS	Radical RT + CT Palliative CT	I / IV	NCCN[5] NCI PDQ[6]	0.03
14	Nasopharyngeal cancer, stage I, distant recurrence, good PS	Palliative CT	IV	NCCN[5] NCI[9]	<0.01
15	Nasopharyngeal cancer, stage I, definitive radiotherapy, recurrence following salvage treatment, good PS	Palliative CT	IV	NCCN[5] NCI[9]	0.00
17	Nasopharyngeal cancer, stage I, definitive radiotherapy, recurrence, unsalvageable disease, good PS	Palliative CT	IV	NCCN[5] NCI[9]	<0.01
20	Nasopharyngeal cancer, stage II, locoregional recurrence, unsalvageable disease, good PS	Palliative CT	III	NCCN[5] NCI[9] BCCA[17]	<0.01
22	Nasopharyngeal cancer, stage II, definitive radiotherapy, recurrence following salvage treatment, good PS	Palliative CT	III	NCCN[5] NCI[9] BCCA[17]	<0.01
23	Nasopharyngeal cancer, stage II, definitive radiotherapy, distant recurrence, good PS	Palliative CT	III	NCCN[5] NCI[9] BCCA[17]	<0.01
25	Nasopharyngeal cancer, stages III and IV, good PS	Radical RT + CT	I	NCCN[5] NCI[9] CCO[21] Cochrane[40]	0.02
27	Oropharyngeal cancer, stages I and II, recurrence, unsalvageable disease, good PS	Palliative CT	IV	NCCN5 NCI[8]	<0.01
29	Oropharyngeal cancer, stages III and IV, good PS	Radical RT + CT/ postoperative RT + CT/ palliative CT	I/I/IV	NCCN[5] NCI[8]	0.05
31	Hypopharyngeal cancer, stages I and II, recurrence, unsalvageable disease, good PS	Palliative CT	IV	NCCN[5] NCI[12] SIGN[25]	<0.01
33	Hypopharyngeal cancer, stages III and IV, good PS	Induction CT/ postoperative RT + CT/ radical RT + CT/palliative CT	II/I/IV	NCCN[5] NCI[12] SIGN[25]	<0.01
35	Laryngeal cancer, stages I and II, recurrence, unsalvageable disease, good PS	Palliative CT	IV	NCCN[5] NCI[7] SIGN[25]	0.01
37	Laryngeal cancer, stages III and IV, good PS	Radical RT + CT/ postoperative RT + CT/ palliative CT	II/I/IV	NCCN[5] NCI[7] SIGN[25]	0.06
39	Paranasal sinus and nasal cavity cancer, locoregional disease, recurrence, unsalvageable disease, good PS	Palliative CT	IV	NCCN[5] NCI[10] BCCA[20]	0.01

(Continued on next page)

Table 1 – continued

Outcome No.	Clinical scenario	Treatment indicated	Level of evidence*	Ref.	Proportion of all head and neck cancer patients
41	Paranasal sinus and nasal cavity cancer, metastatic disease, good PS	Palliative CT	IV	NCCN[5] NCI[10] BCCA[20]	0.01
42	Salivary gland cancer, locoregional disease, distant recurrence, good PS	Palliative CT	IV	NCCN[5] NCI[11]	0.02
44	Salivary gland cancer, metastatic disease, good PS	Palliative CT	IV	NCCN[5] NCI[11]	0.01
Total proportion of patients with primary head and neck cancer in whom chemotherapy is recommended					0.36

Abbreviations: CT, chemotherapy; PS, performance status; NCCN, National Comprehensive Cancer Network; NCI PDQ, National Cancer Institute Physicians Data Query; BCCA, British Columbia Cancer Agency; CCO, Cancer Care Ontario; SIGN, Scottish Intercollegiate Guidelines Network.

* Levels of evidence for indications for chemotherapy: Level I – evidence obtained from a systematic review of all relevant randomised controlled trials; Level II – evidence obtained from at least one properly designed randomised controlled trial; Level III – evidence obtained from well-designed controlled trials without randomisation -these include trials with 'pseudo-randomisation' where a flawed randomisation method was used (e.g. alternate allocation of treatments) or comparative studies with either comparative or historical controls; Level IV – evidence obtained from case series. These are taken from the National Health and Medical Research Council (NHMRC) hierarchy of levels of evidence.[26]

should receive at least one course of chemotherapy during the course of their illness based on the best evidence available, and to compare this with the actual utilisation rates reported. This study was part of a larger project to estimate the optimal chemotherapy utilisation in cancer care.

2. Materials and methods

2.1. *Indications for chemotherapy*

We defined an indication for chemotherapy as a clinical situation in which chemotherapy is the treatment of choice on the basis of superior clinical outcomes in comparison to other treatment modalities (including best supportive care or no treatment). The superiority of chemotherapy over other treatment options could be based on survival, quality of life or toxicity profile. Chemotherapy could be recommended either alone or in combination with radiotherapy or surgery. The lists of drugs classified as chemotherapeutic agents were as defined in SEER*RX (Interactive Antineoplastic Drug Database).[4] The optimal choice of individual drugs or chemotherapy regimens was beyond the scope of this study.

We identified the evidence-based indications for chemotherapy treatment in head and neck cancer from several clinical practice guidelines. The guidelines reviewed were published by the United States National Comprehensive Cancer Network (NCCN)[5] and National Cancer Institute (NCI)[6–12]; the Canadian British Columbia Cancer Agency (BCCA)[13–20] and Cancer Care Ontario (CCO)[21–24] as well as by the Scottish Intercollegiate Guidelines Network (SIGN).[25] The quality of evidence used to justify each of the indications for chemotherapy was adapted from the Australian National Health and Medical Research Council (NHMRC) hierarchy of levels of evidence.[26] In situations where differing guideline recommendations or multiple treatment options exist (e.g. radiotherapy alone versus concurrent chemo-radiation), the guideline recommendation or treatment option with the highest level of evidence was selected.

2.2. *Incidence data (tumour and patient attributes)*

We obtained data on the proportion of tumour and patient attributes for which chemotherapy is indicated from the Australian Institute of Health and Welfare (AIHW),[27] South Australian State Cancer Registry,[28] United States National Cancer Database[29] and published literature. We ranked the quality of data found using a hierarchy shown in Table 2 (as previously described in the optimal radiotherapy utilisation study).[30] In situations where data on the same item were available from multiple sources, the data ranked highest quality were used as the base value in the chemotherapy utilisation tree. In situations where data obtained from multiple sources were ranked of equivalent quality, the larger sample size was chosen.

2.3. *Issue of performance status*

Performance status is an important criterion used in clinical trials and clinical practice to select and stratify eligible patients, as it is a major prognostic factor for survival and predicts benefits from treatment.[31] Chemotherapy is generally recommended only for patients with good performance status (ECOG 0–2).[5] Unfortunately, no specific performance status data were available for the head and neck carcinoma population despite an extensive literature search. Therefore, we estimated the proportion of age-adjusted good performance status patients by combining the Australian Institute of Health and Welfare[32] data on the proportion of head and neck carcinoma by age groups (<55 years old, 55–64 years old, 64–75 years old and >75 years old) with the New South Wales Population Health Survey 2005[27] data on 'difficulty doing work' by each of the corresponding age groups.

Participants in the NSW Population Health Survey were asked about the degree of difficulty that they had experienced in undertaking daily work or activities (no difficulty, little difficulty, some difficulty, much difficulty or unable to carry out daily activities or work) in the past 4 weeks. This scale shows

Table 2 – Head and neck cancer. The incidence of attributes used to define indications for chemotherapy.

Population or subpopulation of interest	Attribute	Proportion of populations with this attribute	Quality of information	Ref.
All registry cancers	Head and neck cancer	0.04	α	AIHW[27]
Head and neck cancer	Good PS	0.79–0.90	α	AIHW.[27]
			δ	NSW population Health survey*,[32]
Head and neck cancer	Lip cancer	0.29	α	AIHW[27]
Head and neck cancer	Oral cavity cancer	0.28	α	AIHW[27]
Head and neck cancer	Nasopharyngeal cancer	0.03	α	AIHW[27]
Head and neck cancer	Oropharyngeal cancer	0.09	α	AIHW[27]
Head and neck cancer	Hypopharyngeal cancer	0.04	α	AIHW[27]
Head and neck cancer	Laryngeal cancer	0.16	α	AIHW[27]
Head and neck cancer	Paranasal sinus and nasal cavity cancer	0.04	α	AIHW[27]
Head and neck cancer	Salivary gland cancer	0.07	α	AIHW[27]
Lip cancer	Distant metastases	0.02	ζ	Vahtsevanos et al.[41]
Lip cancer, locoregional disease	Recurrence	0.15	ζ	Zitsch et al.[42]
Lip cancer, locoregional disease, recurrence	Local	0.75	ζ	Zitsch et al.[42]
Lip cancer, locoregional, disease, local recurrence, salvage treatment	Distant recurrence	0.32	θ	Rowe et al.[43]
Oral cavity cancer	Stages I and II	0.54	γ	Hoffman et al.[1]
Oral cavity cancer, stages I and II	Recurrence	0.36	ζ	Carvalho et al.[44]
		0.19	ζ	Koo et al.[45]
Oral cavity cancer, stages III and IV	Suitable for surgery	0.75	ε	SA Cancer Registry[28]
Oral cavity cancer, stages III and IV, suitable for surgery	Extracapsular nodal extension and/or positive margins	0.28	ζ	Carvalho et al.[44]
Oral cavity cancer, stages III and IV, suitable for surgery, no extracapsular nodal extension and/or positive margins	Recurrence	0.28	ζ	Carvalho et al.[44]
		0.42	ζ	Koo et al.[45]
Oral cavity cancer, all recurrence, salvage treatment	Overall cure	0.14	ζ	Koo et al.[45]
Nasopharyngeal cancer	Stage I	0.08	γ	NCDB[29]
Nasopharyngeal cancer	Stage II	0.21	γ	NCDB[29]
Nasopharyngeal cancer	Stages III and IV	0.71	γ	NCDB[29]
Nasopharyngeal cancer, stage I	Recurrence	0.15	ε	Lee AWM[46]
Nasopharyngeal cancer, stage I, recurrence	Isolated locoregional	0.75	ζ	Chua et al.[47]
		1.00	ζ	Corry et al.[48]
Nasopharyngeal cancer, stage II	Recurrence	0.28	θ	Lee AWM[46]
Nasopharyngeal cancer, stage II, recurrence	Isolated locoregional	0.42	ζ	Chua et al.[47]
		0.43	ζ	Corry et al.[48]
Nasopharyngeal cancer, locoregional recurrence	Salvageable by surgery/radiotherapy	0.66	ε	Yu et al.[49]
Nasopharyngeal cancer, locoregional recurrence, salvageable by surgery/radiotherapy	Recurrence	0.74	ε	Yu et al.[49]
Oropharyngeal cancer	Stages I and II	0.33	γ	Hoffman et al.[1]
		0.17	γ	NCDB[29]
Oropharyngeal cancer, stages I and II	Recurrence following local treatment	0.25	ζ	Selek et al.[50]
		0.45	ζ	Carvalho et al.[44]

(*Continued on next page*)

Table 2 – continued

Population or subpopulation of interest	Attribute	Proportion of populations with this attribute	Quality of information	Ref.
Oropharyngeal cancer, stages I and II, recurrence	Overall cure rate from salvage treatment	0.26	ζ	Selek et al.[50]
Hypopharyngeal cancer	Stages I and II	0.22	γ	Hoffman et al.[1]
		0.17	γ	NCDB[29]
Hypopharyngeal cancer, stages I and II	Recurrence following local treatment	0.31	δ	Hoffman et al.[51]
Hypopharyngeal cancer, stages I and II, recurrence	Overall cure rate from salvage treatment	0.40	ε	Nakamura et al.[52]
Laryngeal cancer	Stages I and II	0.59	γ	Hoffman et al.[1]
Laryngeal cancer, stages I and II	Recurrence following local treatment	0.23	ζ	Johansen et al.[53]
Laryngeal cancer, stages I and II, recurrence	Overall cure rate from salvage treatment	0.49	ζ	Johansen et al.[53]
Paranasal sinus and nasal cavity cancer	Distant metastases	0.14	γ	Ries et al.[54]
Paranasal sinus and nasal cavity cancer, locoregional disease	Recurrence following local treatment	0.52	ε	Dulguerov et al.[55]
Paranasal sinus and nasal cavity cancer, recurrence following local treatment	Overall cure rate from salvage treatment	0.13	ε	Dulguerov et al.[55]
Salivary gland cancer	Distant metastases	0.14	γ	Ries et al.[54]
Salivary gland cancer, locoregional disease	Distant recurrence following local treatment	0.33	ε	Terhaard et al.[56]

Abbreviations: AIHW, Australian Institute of Health and Welfare; NSW, New South Wales; NCDB, National Cancer Database; SA, South Australia; PS, performance status.
Hierarchy for epidemiological data: α, Australian National Epidemiological data; β, Australian State Cancer Registry; γ, epidemiological databases from other large international groups (e.g. SEER); δ, results from reports of a random sample from a population; ε, comprehensive multi-institutional database; ζ, comprehensive single-institutional database; θ, multi-institutional reports on selected groups (e.g. multi-institutional clinical trials; λ, single-institutional reports on selected groups of cases; μ, expert opinion.
* Performance status data are estimated from the general population, and are not specific to head and neck cancer patients.

a reasonable correlation with the Eastern Cooperative Oncology Group (ECOG)[33] scoring scales used to measure performance status. Good performance status (ECOG 0–2) was assumed in those who reported 'no difficulty at all', 'a little bit of difficulty' and 'some difficulty'. Participants who reported 'much difficulty' or who could not do work or carry out daily activities were assumed to have poor performance status, corresponding to ECOG 3–4. As there was some uncertainty about whether respondents with 'some difficulty' should be included in the good performance status group, sensitivity analysis was performed to assess the effect of this uncertainty on the estimated optimal utilisation rate. Estimates of performance status were age adjusted because the incidence and the proportion of good performance status patients vary with age.

2.4. *Statistical analysis*

The robustness of the chemotherapy utilisation model was tested with univariate sensitivity analyses and Monte Carlo simulations. Univariate sensitivity analyses were conducted if the incidence of epidemiological data obtained varied by more than 10% or when there were disagreements between guidelines for a chemotherapy treatment indication. Monte Carlo simulations were performed to assess the effect of varying all the uncertain incidence data identified (greater than 10% difference in incidence data) simultaneously on the overall utilisation rate.

2.5. *Optimal chemotherapy utilisation rate*

The indications for chemotherapy treatment given in Table 1 and the incidence data on the proportion of tumour and patient attributes given in Table 2 were merged using TreeAge Pro 2007 software (version 1.0) to generate an optimal chemotherapy utilisation tree for head and neck carcinoma. Each branch of the chemotherapy utilisation tree represents an important tumour or patient-related attribute that affects the chemotherapy decision. Each terminal branch of the tree shows whether chemotherapy is indicated for each of the specific clinical scenarios as shown in Table 1.

In the utilisation tree, each patient with an indication for chemotherapy treatment was only counted once (i.e. the tree was terminated at the point of chemotherapy being recommended), even if they may have subsequent indications during the course of their illness. This was to standardise the comparison of the optimal rate with reported actual rates of chemotherapy utilisation (defined as the number of patients treated by chemotherapy for the first time divided by the incidence of specific cancers during a period).

The optimal utilisation rate was calculated from the summation of the incidence of each indication for chemotherapy. This was then compared with actual chemotherapy utilisation rates reported in the literature.

The epidemiological data and indications for chemotherapy used in our model were externally reviewed by multidisciplinary experts from the New South Wales Head and Neck Oncology Group, Victoria Cooperative Oncology Group (Head and Neck Cancer) and Australian and New Zealand Head

and Neck Society to ensure clinical validity. Appropriate changes were made based on the feedback received.

3. Results

The optimal chemotherapy utilisation tree for head and neck carcinoma (cancer of the lip, oral cavity, nasopharynx, oropharynx, hypopharynx, larynx, salivary gland, paranasal sinus and nasal cavity) is shown in Fig. 1. Each branch represents a patient or tumour attribute that defines the clinical situation of whether chemotherapy is indicated or not. The description of the attributes is located above each branch of the utilisation tree with the corresponding epidemiological incidence data on the proportion of that attribute located below that branch.

There were 45 possible outcomes in the chemotherapy utilisation tree. Chemotherapy was indicated in 24 of the possible outcomes identified (listed in Table 2). The optimal chemotherapy utilisation rate for head and neck carcinoma, i.e. the proportion of all patients with head and neck carcinoma who should receive chemotherapy at least once during the course of their illness was 36%. The optimal chemotherapy utilisation rates by subsites were as follows: lip (8%), oral cavity (40%), nasopharynx (69%), oropharynx (66%), hypopharynx (74%), larynx (43%), salivary gland (48%), paranasal sinus and nasal cavity (38%).

There were seven uncertain items identified. Univariate sensitivity analyses were performed to assess the difference in the optimal chemotherapy utilisation rate with the variation of the following proportions: patients with good performance status (0.79–0.90), stage I and II oral cavity cancer (0.19–0.36), stage I and II oropharyngeal cancer (0.17–0.33), recurrence rate of stage III and IV oral cavity cancers (0.28–0.42), recurrence rate of stage I and II oral cavity cancers (0.19–0.36), locoregional recurrence of stage I nasopharyngeal cancer (0.75–1.0) and if chemo-radiation was indicated for stage II nasopharyngeal cancer (0–1.0). The tornado diagram (see Fig. 2) illustrates the overall effect of all the variables described above on the optimal utilisation rate. The range of the optimal chemotherapy utilisation rates of head and neck carcinoma was 31–37%.

Monte Carlo analysis was also performed to assess the overall effect of simultaneously varying all the uncertain data items on the optimal chemotherapy utilisation rate. Based on 10,000 simulations using the following variables (proportions as previously described): stage I and II oral cavity cancer, stage

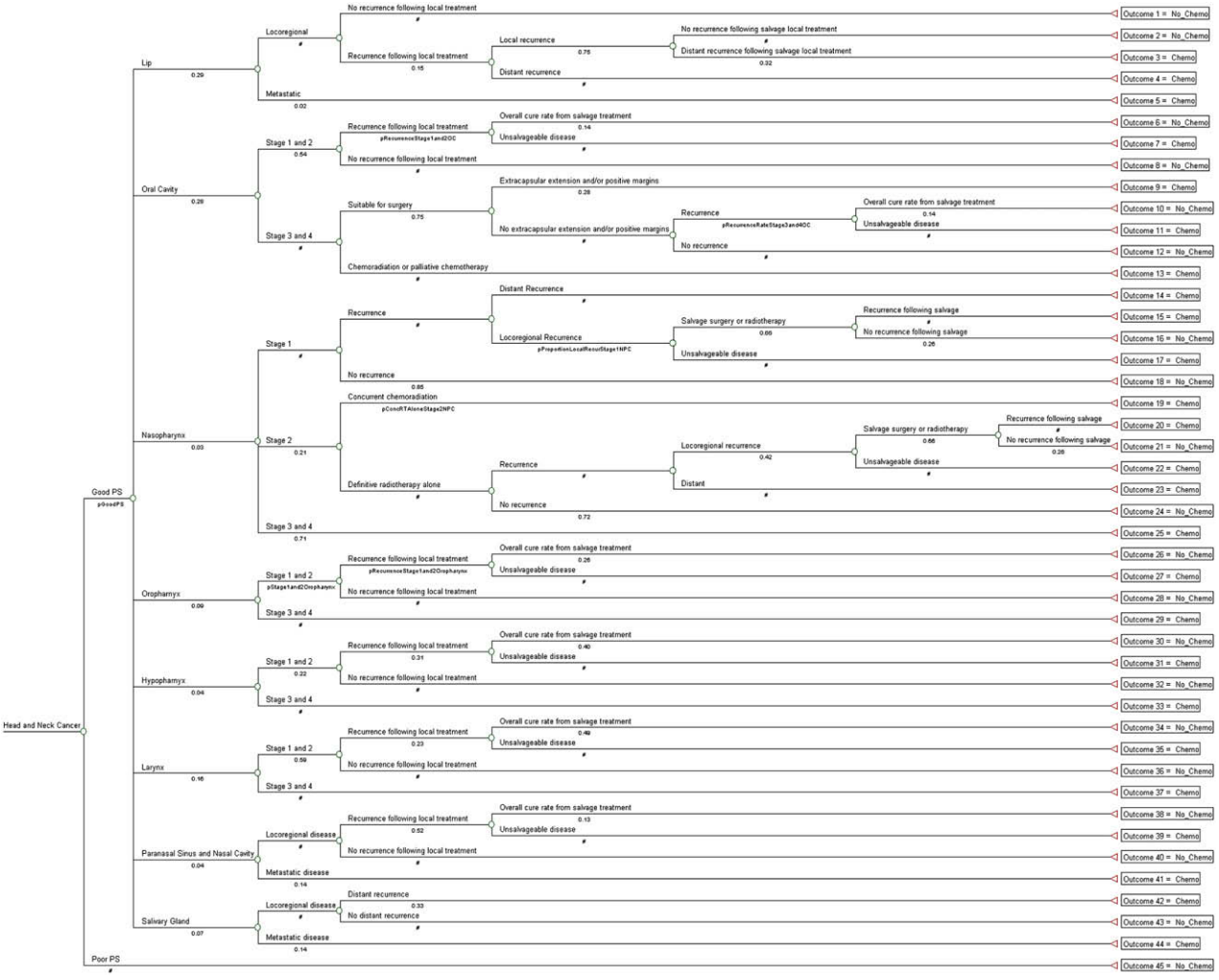

Fig. 1 – Optimal chemotherapy utilisation tree for head and neck cancer.

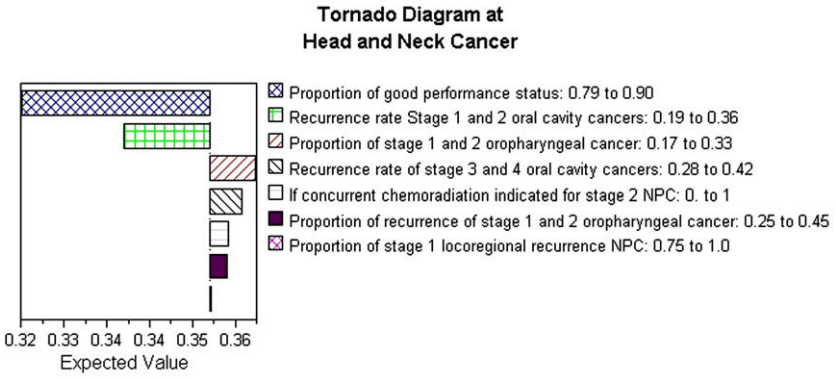

Fig. 2 – Tornado analysis of the variation in data and uncertainty in evidence for chemotherapy in head and neck cancer. A description of the interpretation of the tornado diagram is provided in the sensitivity analysis section.

Table 3 – Comparison of optimal and actual chemotherapy utilisation rates for head and neck carcinoma.

	Optimal utilisation (%)		Actual first course of treatment utilisation (%)			
	Any time	First course of treatment				
Source	–	–	NCDB (US)[1]		South Australia[28]	NYCRIS (UK)[2]
Year(s) survey	–	–	1985–1989	1990–1994	1987–1998	2003
No. of patients	–	–	118292	176730	789	858
All sites	36	23	15	17	–	12*
Lip	8	2	1		0	–
Oral cavity	40	19	9		8	–
Nasopharynx	69	67	50		21	–
Oropharynx	66	60	22		27	–
Hypopharynx	74	70	24		43	–
Larynx	43	37	7		–	–
Paranasal sinus and nasal cavity	48	13	19		–	–
Salivary gland	38	13	10		3	–

NCDB, National Cancer Database; NYCRIS, Northern and Yorkshire Cancer Registry and Information Service; US, United States and UK, United Kingdom.
* Excluding thyroid carcinoma.

I and II oropharyngeal cancer, recurrence rate of stage III and IV oral cavity cancers, recurrence rate of stage I and II oral cavity cancers and locoregional recurrence of stage I nasopharyngeal cancer, the optimal utilisation rate was 35% (95% confidence intervals 33–38%).

3.1. *Comparison with actual practice*

Actual chemotherapy utilisation rates in head and neck carcinoma have been reported by the South Australian Cancer Registry,[28] United States National Cancer Database (NCDB)[1] and United Kingdom Northern and Yorkshire Cancer Registry and Information Service (NYCRIS).[2] The actual chemotherapy utilisation rates of head and neck carcinoma (12–17%)[1,2] were lower than the optimal rate of 36% (see Table 3). However, the actual rates published were for the time periods of 1984–1989,[1] 1990–1994[1] and 2003,[2] and may not reflect the current practice as further evidence for chemotherapy has emerged over the past 20 years. Fig. 3 shows the cumulative proportion of cases with an indication for chemotherapy over time, which allows for a more accurate and valid comparison with the historical actual rates. The actual utilisation rate of chemotherapy (17%) in the United States[1] was similar to the estimated optimal rate (15%) for the period of 1990–1994. In contrast, the actual utilisation rate of chemotherapy of 13% reported by NYCRIS for the year 2003 was much lower than the optimal rate of 36% for a similar time period, raising the concern of under-utilisation.

When analysed by the head and neck carcinoma subsites, the actual utilisation rates were also much lower than each of the corresponding optimal utilisation rates.[1,28] We interpreted the large differences seen with some caution as majority of these studies reported the actual chemotherapy utilisation rates based on the first course of treatment only, which does not account for any chemotherapy given following recurrent disease. However, the actual utilisation rates reported were also lower by 5–11% when compared to the estimated optimal utilisation rate for the first course of treatment only of 23% (see Table 3).

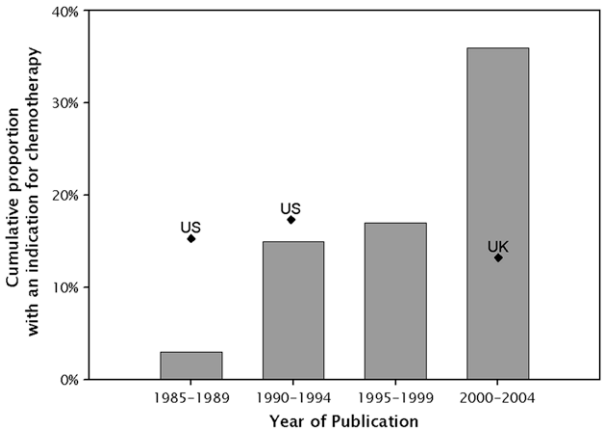

Fig. 3 – Comparison of the proportion with an indication for chemotherapy over time with actual chemotherapy utilisation rates (♦) for the US.

For lip and salivary gland carcinomas, where the only indication of chemotherapy was for patients with metastatic disease, the actual utilisation rate approximated the optimal utilisation rate (1% and 3%, respectively). The greatest discrepancies between the optimal and actual chemotherapy utilisation rates were seen in the head and neck carcinoma subsites of nasopharynx, oropharynx, hypopharynx and larynx, where the difference was 17–46%.

4. Discussion

Our evidence-based model of optimal chemotherapy utilisation demonstrated that 36% of patients with head and neck carcinoma should receive chemotherapy at least once during the course of their illness. Despite several uncertain items identified, both the univariate sensitivity analyses and Monte Carlo simulations confirmed the robustness of the chemotherapy utilisation model. The 95% confidence interval showed only a small variation in the optimal chemotherapy utilisation of 33–38%.

The strength of this model included the use of evidence-based treatment guidelines to develop indications of chemotherapy in head and neck carcinoma. The complexities of clinical (e.g. performance status) and pathological factors (e.g. stage) that may affect the decision of chemotherapy use in clinical practice were also included in the model. The combination of the above-mentioned parameters sets a realistic benchmark of what the ideal chemotherapy utilisation rate for a population of head and neck carcinoma should be. The ability of the model to analyse the optimal chemotherapy utilisation rates by tumour subsites was also an important feature. This is because head and neck carcinoma are a heterogenous population which consists of several subsites with different indications of chemotherapy treatment, and therefore different chemotherapy utilisation rates.

However, our findings should be considered in the light of several limitations in our study. Firstly, co-morbidity has a major impact on the overall survival and treatment selection of patients with head and neck cancer.[34] Severe co-morbidities are associated with poorer overall survival, increased postoperative complications and receipt of less intensive treatments.[35] In a prospective cohort study, Piccirillo[34] documented the proportions of head and neck cancer patients with moderate and severe co-morbidities at 16% and 5%, respectively. However, the current practice guidelines do not provide specific guidance on the effect of co-morbidities in their recommendations for chemotherapy, but rather use performance status as an indicator of overall fitness. For example, the NCCN guidelines recommend chemotherapy for patients with good performance status (ECOG 0 and 1), but could also be considered in those with borderline performance status (ECOG 2). In our model, if patients with borderline and poor performance status (ECOG 2–4) were not indicated for chemotherapy, then the optimal utilisation rate falls to 32%. Secondly, our estimates of performance status were derived from the general population, and this could lead to an overestimation of the optimal rate as patients with head and neck tend to be more frail. Thirdly, patient refusal of chemotherapy may be a valid reason for non-receipt of guideline recommended treatment. We were unable to factor this into the model as there were no published studies available on patient preferences for chemotherapy in head and neck cancer. Several studies have shown that patients with breast cancer were willing to accept chemotherapy treatment for small benefits.[36,37] Finally, we assumed that patients aged 71 years and over with good performance status with an indication for chemotherapy were fit enough for treatment, which may overestimate the optimal utilisation rate. Although the guidelines do not exclude the elderly cohort (from receiving chemotherapy), population-based studies from the Eindhoven Cancer Registry[38] show that they have a higher rate and number of co-morbidities when compared with their younger counterparts. These limitations can be incorporated in the model in future studies.

Potential reasons for the differences seen in the optimal and actual chemotherapy utilisation rates include the recent expansion of the role of chemotherapy to include concurrent chemo-radiation in the postoperative setting due to emerging data.[39] This may account for some of the shortfalls seen, as the actual utilisation data from the studies above were reported prior to the publication of the data supporting this treatment. However, this newer indication alone is unlikely to be the sole reason for the significant differences seen between optimal and actual practice. Other possible explanations for the under-utilisation of chemotherapy in head and neck carcinoma may include under-referrals, lack of access to chemotherapy treatment facilities, patient refusal and clinician bias. These are not well studied in the current literature.

In conclusion, this evidence-based model showed that the optimal chemotherapy utilisation in head and neck carcinoma is 36%. The cumulative proportion of head and neck patients who are indicated to have chemotherapy has also risen significantly over the past 20 years. Recent actual utilisation rate of chemotherapy appears to be lagging behind the optimal rate. Large population-based studies are required to further assess the magnitude and the potential reasons for the differences seen between the current and ideal practice. Potential treatment benefits for achieving the best local control

and survival in patients with head and neck carcinoma are lost when evidence from trials are not translated into clinical practice.

Conflict of interest statement

None declared.

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