



Healthier
**Lancashire &
South Cumbria**

**Cancer
Alliance**

Head and Neck Cancer Management Guidelines Version 2 2019

**Created V1
To be Reviewed
Created V2
To be Reviewed**

**February 2016
February 2018
May 2019
May 2021**

Introduction:

In year 2008, there were 8600 new Head and Neck cancers diagnosed in the United Kingdom. The annual mortality of 2900 per annum was expected. There were marked regional variations in the incidence of Head and Neck cancers, with rates ranging from 8 per 100,000 in the Thames and Oxford regions to 13-15 per 100,000 in Wales and the North West. The Head and Neck cancer may be caused by different factors depending on the tumor type and location. Head and Neck cancers are traditionally associated with older men with history of excessive smoking and alcohol consumption. However, the incidence in the younger patients of both sexes is increasing. This is due to the increasing incidence of HPV related Oropharyngeal cancers. The incidence of Oropharyngeal cancer (OPC) has increased dramatically. In England, the incidence of OPC has more than doubled the decade between 1995 to 2006. Recent figures show that incidence of OPC has almost doubled again between 2006 and 2010. In Scotland, incidence of OPC is the fastest rising of all cancers. The proportion of OPC caused by HPV has more than doubled over the past decade to 70%. The treatment approaches have changed over the last few decades with increasing use of Chemoradiotherapy and IMRT (Intensity Modulated Radiotherapy). Current research is examining de-escalation and escalation approaches to improve the treatment outcomes for patients with Head and Neck cancers.

Scope:

This document is created for the perusal of Lancashire and South Cumbria Head & Neck Multi-Disciplinary Team Meetings (MDTs). There are two Head & Neck MDTs in the Network : one at East Lancashire Hospitals Trust and one that is hosted from Lancashire Teaching Hospitals Trust (LTHT) covering the populations of LTHT, Blackpool Teaching Hospitals Trust and University Hospitals of Morecambe Bay Trust. Both MDTs meet weekly and the LTHT hosted MDT is conducted with participants linking in via teleconference to participate in the MDT on every Tuesday mornings. The guidelines cover most aspects of Head and Neck cancer management that are undertaken by the members of the MDT. It is anticipated that these guidelines will be updated every 2-3 years.

Sources:

These guidelines are based on the recommendations of ENT UK (BAHNO), NICE Guidelines, SIGN and NCCN Guidelines.

Table of Contents

Page

1.	Diagnostic Work-up and Pre-treatment evaluation.....	4
2.	Follow up recommendations.....	5
3.	Histologic Grading, Incidence and Distribution of nodes in HNSCC.....	6
4.	Neck nodal levels and Nodal Staging.....	7
5.	Lip and Oral cancer T staging and Lip cancer Treatment.....	8
6.	Oral cancers.....	9
7.	Oropharyngeal cancers.....	10
8.	Larynx and Hypopharynx cancers T staging.....	11
9.	Larynx and Hypopharynx Treatment.....	12
10.	Nasopharyngeal cancers.....	13
11.	Ethmoid tumours treatment, Nasal & Ethmoid T staging.....	14
12.	Maxillary tumours treatment and T staging.....	15
13.	Neck nodes with unknown Primary.....	16
14.	Salivary Gland Tumours.....	17
15.	Mucosal Melanoma.....	18
16.	Head and Neck sarcomas.....	19
17.	Recurrent and rare Head and Neck tumours.....	20
18.	Chemotherapy Algorithms.....	22
19.	Appendix 1: ACE 27 UK values.....	23
20.	Appendix 2: Charlson Index.....	24
21.	Appendix 3: Post CRT/RT neck management.....	25
22.	Appendix 4: Sarcoma TNM and subtype management guidelines.....	26

Diagnostic Work-up and Pre-treatment evaluation:

- History with documentation of
 - WHO performance Status
 - Comorbidities (Adult Comorbidity evaluation 27 or Charlson Index). (Appendix 1 & 2)
 - History of Smoking (E.g. 10 pack years or more) and Alcohol consumption
- Direct inspection of Upper Aero-Digestive Tract (Clinical photograph for MDT presentation where applicable)
- Neck Examination
- US +/- FNA of neck nodes if suspicious. US scan can detect 20% of involved neck nodes that were normal on clinical assessment.
- Biopsy/FNA. Ideally biopsies are done after scans if possible to avoid post biopsy oedema and upstaging of primary tumour.
- MRI Head and Neck (For tumours of Oral cavity, Oropharynx and Nasopharynx), CT Neck and Chest. If landmark CT scans done for sino-nasal tumours an MRI scan is also recommended
- In Head and Neck Squamous cancers with an unknown primary (Neck node with squamous cancer with no obvious primary on clinical examination), a PET/CT must be done before any biopsies or tonsillectomies. In unknown primaries, PET/CT can help detect a primary in 1/3rd of cases. PET/CT can also detect distant metastases. MRI head and neck is also recommended.
- Dietetic and Speech therapy assessment in appropriate cases. If weight loss is in excess on 10% of baseline body weight, nutritional intervention is recommended. Consider NG/RIG feeding
- HPV testing recommended for all cancers of oropharynx using p16 immunohistochemistry (locally). HPV DNA testing should be considered to confirm HPV status (Sent to the central lab). This is increasingly becoming a prerequisite for planning treatment for patients and also in assessing eligibility for clinical trials.
- In patients suspected to have lymphoma an excision of lymph node is recommended and FNA is not considered to be an ideal test
- Avoid lymph node excision if squamous cancer suspected unless there is no other alternative options. However, occasionally lymph node or lump excision may be necessary to obtain diagnosis.
- If Carotid body tumour suspected, discuss appropriate imaging in MDT prior to any intervention
- Squamous cancer in a branchial cyst is a diagnosis of exclusion. In the context of HPV positive cancers, which tend to present with large cystic nodal metastases (Poorly differentiated squamous cancers) especially in the absence of an obvious primary (occult primary) or with a relatively small primary, it is recommended to discuss scans in MDT prior to excision of neck masses
- For suspected salivary gland malignancies, MRI head and neck and CT chest is recommended. Avoid core biopsies in suspected Salivary gland malignancies. FNA is recommended instead.
- Dental assessment for tumours of Oropharynx and Nasopharynx. Dental assessment is not routinely required for early larynx/supraglottic cancers.

Follow up recommendations:

- The aim of follow-up is the early detection of potentially curable loco-regional recurrence and second tumours.
- A shared care follow up between surgical teams and oncology is to be adopted, when it's feasible these follow up assessments are undertaken closer to home.
- In the **first year** of completion of treatment, Patients are seen in the OP clinic **every 4-6 weeks** until resolution of acute toxicity.
- Post CRT imaging is done at 3 to 4 months after completion of treatment. This is ideally done with an MRI scan. While these assessments have a predictive value for treatment outcomes, these are also useful in assessing for any salvage therapy in residual/recurrent/progressive tumours. (Appendix 3)
- For patients with residual nodal disease on post treatment MRI / CT, arrange a PET CT following MDT discussion.
- Post CRT biopsies and FNAs are difficult to evaluate as is post CRT Ultra Sound assessment of residual neck nodes, which were abnormal/involved previously.
- **Second Year:** Outpatient clinic review **every 2-3 months** with clinical assessment and fibre-optic scope examination as deemed necessary. Alternate appointments between surgical and oncology clinics. (nearer home if possible)
- **From year 3 onwards:** Recommended duration of follow up is for a total of 5 years after completion of treatment. **Every 4-6 months** to alternate between surgical and oncology teams. Aim to discharge patients at the end of the 5-year period in the absence of significant treatment related morbidity or any other suspicious symptoms.
- Thyroid function test (serum thyroid-stimulating hormone—TSH—levels) in patients with irradiation to the neck is recommended at 1, 2 and 5 years.
- EBV DNA monitoring in patients with nasopharyngeal cancers.
- No routine follow up scans are recommended in the absence of any concerning symptoms or signs outside of clinical trials
- Chest X-ray may be included on a yearly basis for follow up.

Histologic Grading of HNSCC:

Histologic grade (G)	
GX	Grade cannot be assessed
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated
G4	Undifferentiated

Incidence and distribution of regional nodal involvement in HNSCC:

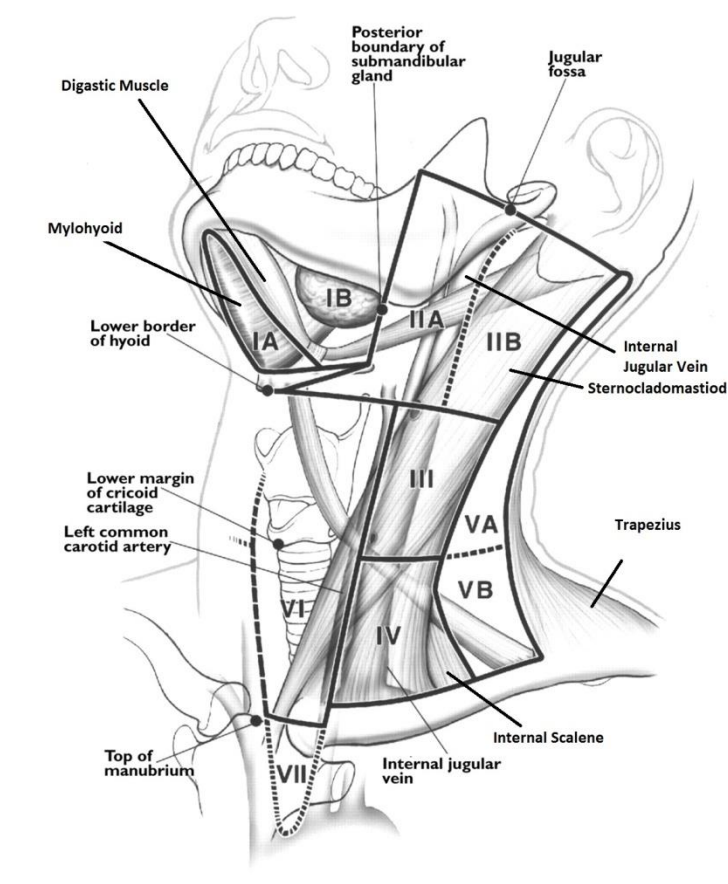
Table 42.3		INCIDENCE AND DISTRIBUTION OF REGIONAL METASTASIS FOR LEVELS I-V FOR CLINICALLY NO NECK.				
Tumor Site	Levels Involved (%)					
	I	II	III	IV	V	
Oral cavity	20	17	9	3	0.5	
Oropharynx	2	25	19	8	2	
Hypopharynx	0	13	13	0	0	
Larynx	5	19	20	9	2.5	

(See references: Bataini, Byers, Candela Chao, Lindberg, Shah, Shah). Gregoire V, Coche E, Cosnard et al, Radiotherapy and Oncology, 2000;56 (2):135-150.

Table 42.4		INCIDENCE AND DISTRIBUTION OF REGIONAL METASTASIS FOR LEVELS I-V FOR CLINICALLY N+ NECK.				
Tumor Site	Levels Involved (%)					
	I	II	III	IV	V	
Oral cavity	48	39	31	15	4	
Oropharynx	15	71	42	27	9	
Hypopharynx	10	75	72	45	11	
Larynx	6	61	54	30	6	
Nasopharynx	13	95	60	21	44	

(See references: Bataini, Byers, Candela Chao, Lindberg, Shah, Shah, Sham). Gregoire V, Coche E, Cosnard et al, Radiother and Oncology, 2000;56 (2): 135-150.

Neck Nodal levels:



Nodal Staging for Oral, Oropharynx, Larynx, Hypopharynx, Nasal/Ethmoid, Maxillary, Major Salivary Gland cancers:

- NX: Regional lymph nodes cannot be assessed
- N0: No regional lymph node metastasis
- N1: Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension
- N2: Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
- N2a: Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension
- N2b: Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension
- N2c: Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension
- N3: Metastasis in a lymph node more than 6 cm in greatest dimension

Lip and Oral cancers (T Staging):

T X	Primary tumour cannot be assessed
T 0	No evidence of primary tumour
T is	Carcinoma <i>in situ</i>
T1	Tumour 2 cm or less in greatest dimension
T2	Tumour more than 2 cm but not more than 4 cm in greatest dimension
T3	Tumour more than 4 cm in greatest dimension
T4a	Moderately advanced local disease*

Lip: Tumour invades through cortical bone, inferior alveolar nerve, floor of mouth, or skin of face (of chin or nose)

Oral cavity: Tumour invades adjacent structures (e.g. through cortical bone [mandible or maxilla] into deep [extrinsic] muscle of tongue [genioglossus, hyoglossus, palatoglossus, and styloglossus], maxillary sinus, skin of face)

T4b Very advanced local disease
Tumour invades masticator space, pterygoid plates, or skull base and/or encases internal carotid artery

*Note: Superficial erosion alone of bone/tooth socket by gingival primary is not sufficient to classify a tumour as T4.

1. Cancers of Lip:

T1, T2 N0:

- Resection (if positive margins or PNI or LVI for re-resection or RT), Neck Dissection not routinely recommended.
- RT

T3, T4a N0

- Resection of primary +/- ipsilateral ND or
- CRT or RT if not surgical candidate

T3, T4a N1, N2, N3

- Resection of primary with ipsilateral ND +/- Contralateral ND or
- CRT or RT if not surgical candidate

T3, T4a N2c

- Resection of primary with bilateral ND or
- CRT or RT if not surgical candidate

T4b Any N or Irresectable Disease or Unfit for Surgery:

- CRT or Induction chemotherapy followed by CRT or RT in PS 0, 1.
- RT +/- Chemotherapy in PS 2.
- BSC or Single agent chemotherapy or RT in PS 3.

Adjuvant Therapy (Post-operative)¹:

- RT or CRT
- CRT (For age < 70 years with PS 0,1) recommended for High risk pathology: Margins positive defined as resection margin <1mm or Nodes with ECS
- Discuss adjuvant RT for Intermediate/Low risk pathology: Multiple nodes, T4, PNI, LVI, High Grade histology, Non (dis) cohesive invasive front, close resection margin defined as margin <5mm. Consider post-operative RT when 2 or more low risk factors present. (Consider RT if gross perineural invasion present)

¹ If margins < 1mm or Positive consider Re-resection if feasible.

2. Oral Cancers:

2 a. Early Stage Oral Cancers:

T1, T2 N0 (Stage 1 and 2):

- Aim for single modality treatment.
- Surgery remains the mainstay of treatment of Oral Cancers.
- Surgical resection of primary tumour and appropriate reconstruction as deemed appropriate. Selective neck dissection (Unilateral or Bilateral) depending on tumour thickness and location.
- Radiotherapy can be offered on the basis of organ/function preservation, patient and/or physician preference and performance/functional status.

2 b. Advanced stage Oral cancers:

T3, T4 N0, T1-4 N+ M0 (Stage 3 and 4):

- If resectable:
 - Resection of primary, Neck Dissection, Reconstruction plus post-operative adjuvant RT or CRT depending on prognostic risk factors
- If not resectable or medically inoperable due to co-morbidities and/or patient/physician choice (e.g. unacceptable functional outcome post resection):
 - Chemoradiotherapy or RT plus Cetuximab
 - Radical RT alone if not suitable for concurrent CRT

2 c. M1 disease: Systemic chemotherapy plus or minus RT for palliation

Adjuvant Therapy (Post-operative)²:

- RT or CRT
- CRT (For age < 70 years with PS 0,1) recommended for High risk pathology: Margins positive defined as resection margin <1mm or Nodes with ECS
- Discuss adjuvant RT for Intermediate/Low risk pathology: Multiple nodes, T4, PNI, LVI, High Grade histology, Non (dis) cohesive invasive front, close resection margin defined as margin <5mm. Consider post-operative RT when 2 or more low risk factors present. (Consider RT if gross perineural invasion present)

² If margins < 1mm or Positive consider Re-resection if feasible.

3. Oropharyngeal Cancers: (HPV testing recommended in all cases)

Oropharynx: (T staging)

- T X: Primary tumour cannot be assessed
- T 0: No evidence of primary tumour
- T is: Carcinoma *in situ*
- T1: Tumour 2 cm or less in greatest dimension
- T2: Tumour more than 2 cm but not more than 4 cm in greatest dimension
- T3: Tumour more than 4 cm in greatest dimension or extension to lingual surface of epiglottis
- T4a: Moderately advanced local disease: Tumour invades the larynx, extrinsic muscle of tongue, medial pterygoid, hard palate, or mandible*
- T4b: Very advanced local disease: Tumour invades lateral pterygoid muscle, pterygoid plates, lateral nasopharynx, or skull base or encases carotid artery

*Note: Mucosal extension to lingual surface of epiglottis from primary tumours of the base of the tongue and vallecula does not constitute invasion of larynx.

3 a. Early Oropharyngeal cancers:

T1, T2, N0 (Stage 1 and 2):

- Radical Radiotherapy (Single Modality Treatment)
- Surgery (Trans oral laser resection) in the context of Clinical Trial or with appropriate arrangements for audit and governance agreed by the MDT.
- Tonsillectomy (conventional) on its own is not deemed a curative treatment.

3 b. Advanced Oropharyngeal cancers:

T3, T4 N0, T1-T4 N+ M0 (Stage 3 and 4):

- Chemoradiotherapy (under 70 years of age)
- Induction Chemotherapy (TPF or PF) followed by Chemoradiotherapy for T4 disease or N3 and Bulky N2 disease
- Radical Radiotherapy or Radical RT plus Cetuximab if not suitable for Cisplatin based concurrent Chemoradiotherapy
- Radiotherapy alone if over 70 years of age or if not suitable for Concurrent Chemoradiotherapy
- Neck dissection if residual neck (after appropriate clinical and radiological assessment) disease after CRT/RT
- Upfront neck dissection for bulky neck especially in HPV-ve (with small volume primary or if primary tumour de-bulked) disease if patient not suitable for Induction chemotherapy/CRT.
- Surgery to primary and ND (Trans oral laser resection) in the context of MDT agreed clinical trial or with appropriate arrangements for audit and governance agreed by the MDT.

3 c. M1 disease:

- Systemic chemotherapy plus or minus RT for palliation

Adjuvant Therapy (Post-operative):

- RT or CRT
- CRT (For age < 70 years with PS 0,1) recommended for High risk pathology: Margins positive defined as resection margin <1mm or Nodes with ECS
- Discuss adjuvant RT for Intermediate/Low risk pathology: Multiple nodes, T4, PNI, LVI, High Grade histology, Non (dis) cohesive invasive front, close resection margin defined as margin <5mm. Consider post-operative RT when 2 or more low risk factors present. (Consider RT if gross perineural invasion present)

4. Larynx and Hypopharynx cancers: (T staging)

Supraglottis

- T1: Tumour limited to one subsite of supraglottis with normal vocal cord mobility
- T2: Tumour invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of piriform sinus) without fixation of the larynx
- T3: Tumour limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic tissues, paraglottic space, and/or with minor thyroid cartilage erosion (e.g., inner cortex)
- T4a: Tumour invades through the thyroid cartilage and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), strap muscles, thyroid, oesophagus
- T4b: Tumour invades prevertebral space, mediastinal structures, or encases carotid artery

Glottis

- T1: Tumour limited to vocal cord(s) (may involve anterior or posterior commissure) with normal mobility
- T1a: Tumour limited to one vocal cord
- T1b: Tumour involves both vocal cords
- T2a: Tumour extends to supraglottis and/or subglottis with normal vocal cord mobility
- T2b: Tumour extends to supraglottis and/or subglottis with impaired vocal cord mobility
- T3: Tumour limited to larynx with vocal cord fixation and/or invades paraglottic space, and/or with minor thyroid cartilage erosion (e.g. inner cortex).
- T4a: Tumour invades through the thyroid cartilage, or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), strap muscles, thyroid, Oesophagus
- T4b: Tumour invades prevertebral space, mediastinal structures, or encases carotid artery

Subglottis

- T1: Tumour limited to subglottis
- T2: Tumour extends to vocal cord(s) with normal or impaired mobility
- T3: Tumour limited to larynx with vocal cord fixation
- T4a: Tumour invades through cricoid or thyroid cartilage and/or invades tissues beyond the larynx, e.g., trachea, soft tissues of neck including deep/extrinsic muscle of tongue (genioglossus, hyoglossus, palatoglossus, and styloglossus), strap muscles, thyroid, oesophagus
- T4b: Tumour invades prevertebral space, mediastinal structures, or encases carotid artery

Hypopharynx:

- T1: Tumour limited to one subsite of hypopharynx and/or 2 cm or less in greatest dimension
- T2: Tumour invades more than one subsite of hypopharynx or an adjacent site, or measures more than 2 cm but not more than 4 cm in greatest diameter without fixation of hemilarynx
- T3: Tumour more than 4 cm in greatest dimension or with fixation of hemilarynx or extension to Oesophagus
- T4a: Moderately advanced local disease: Tumour invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, or central compartment soft tissue**
- T4b: Very advanced local disease: Tumour invades prevertebral fascia, encases carotid artery, or involves mediastinal structures

**Note: Central compartment soft tissue includes prelaryngeal strap muscles and subcutaneous fat.

Larynx and Hypopharynx Treatment:

4 a. Carcinoma in situ:

- Laser resection or RT
- Recurrent severe dysplasia or Carcinoma in situ after previous laser resections – consider radiotherapy

4 b. Early Tumours (T1, T2 N0):

- T1a Glottic cancers: Laser resection where anterior commissure not involved or Radical RT if anterior commissure extension or if limited access for laser resection
- T1b and T2: Radical RT (anterior commissure extension or if limited access for laser resection)
- If supraglottic or subglottic extension and risk for subclinical nodal involvement: IMRT (55-65 Gray to Primary and 50 - 60 Gray for elective nodal irradiation)
- For tumours of Hypopharynx: Radical RT +/- Chemotherapy or Cetuximab (if not suitable for Concurrent chemotherapy)
- In selected cases partial open/endoscopic (conservative) resection is an option if expertise is available

4 c. T3 N0 M0:

- Patient PS 0-1, Age < 70: Organ preservation with CRT, or RT if not fit for systemic concurrent therapy or Induction chemotherapy followed by definitive CRT/RT
- Total Laryngectomy (or Pharyngo-laryngectomy) with ipsilateral hemithyroidectomy. Aim for single modality treatment. However, if PORT anticipated, omit neck dissection in view of increased morbidity from combined surgery and RT
- In selected cases conservative resection +/- ND is an option if local expertise/clinical trial is available

4 d. Advanced Cancers (T3 N+ M0):

- Aim for organ preservation with Concurrent Chemoradiotherapy (or Cetuximab) +/- Induction chemotherapy in patients with good PS (0-1).
- Induction chemotherapy with TPF or PF (Veterans regimen) and re-assess (Clinical and Radiological) after 2-3 cycles:
 - If responded continue with Organ preservation (CRT)
 - If no response or if disease progression - for laryngectomy
- Total Laryngectomy with ipsilateral thyroidectomy plus ND (Unilateral or Bilateral)

4 e. Advanced Cancers:

T4a N0, N+, M0:

- Total Laryngectomy or Pharyngo-laryngectomy with Neck dissection and appropriate reconstruction if necessary followed by adjuvant CRT or RT depending on post-operative pathological assessment.
 - T4a N0: Total Laryngectomy and thyroidectomy +/- ND (unilateral or bilateral)
 - T4a N1: Total Laryngectomy and thyroidectomy + ipsilateral ND (+/- contralateral ND)
 - T4a N2-N3: Total Laryngectomy, Thyroidectomy and ipsilateral or Bilateral ND
- If patient declines surgery: CRT/RT/Induction chemotherapy followed by CRT/RT depending on PS.

T4b, (Irresectable Disease):

- PS 0, 1 Some PS2: CRT, RT, Induction chemotherapy followed by RT or CRT
- PS 2, 3: Palliative Chemotherapy (Single agent) or Palliative RT or BSC

4 f. M1 disease: Systemic chemotherapy plus or minus RT for palliation/Local control

4 g. NET/Atypical carcinoids: Ki 67 index to Grade tumour.

- Surgery (Conservative if possible).
- RT/systemic therapy in high grade tumours (small cell histologies)

Adjuvant Therapy (Post-operative):

- RT or CRT
- CRT (For age < 70 years with PS 0,1) recommended for High risk pathology: Margins positive defined as resection margin <1mm or Nodes with ECS
- Discuss adjuvant RT for Intermediate/Low risk pathology: Multiple nodes, T4, PNI, LVI, High Grade histology, Non (dis) cohesive invasive front, close resection margin defined as margin <5mm. Consider post-operative RT when 2 or more low risk factors present. (Consider RT if gross perineural invasion present)

5. Nasopharyngeal cancers:

T staging:

- T X: Primary tumour cannot be assessed
 - T 0: No evidence of primary tumour
 - T is: Carcinoma *in situ*
 - T1: Tumor confined to the nasopharynx, or tumour extends to oropharynx and/or nasal cavity without parapharyngeal extension*
 - T2: Tumor with parapharyngeal extension*
 - T3: Tumor involves bony structures of skull base and/or paranasal sinuses
 - T4: Tumor with intracranial extension and/or involvement of cranial nerves, hypopharynx, orbit, or with extension to the infratemporal fossa/masticator space
- *Note: Parapharyngeal extension denotes posterolateral infiltration of tumour.

N Staging: The distribution and the prognostic impact of regional lymph node spread from nasopharynx cancer, particularly of the undifferentiated type, are different from those of other head and neck mucosal cancers and justify the use of a different N classification system.

- NX: Regional lymph nodes cannot be assessed
- N0: No regional lymph node metastasis
- N1: Unilateral metastasis in cervical lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa, and/or unilateral or bilateral, retropharyngeal lymph nodes, 6 cm or less, in greatest dimension*
- N2: Bilateral metastasis in cervical lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa*
- N3: Metastasis in a lymph node(s)*, > 6 cm and/or to supraclavicular fossa
- N3a: More than 6 cm in dimension
- N3b: Extension to the supraclavicular fossa**

*Note: Midline nodes are considered ipsilateral nodes.

**Supraclavicular zone or fossa is relevant to the staging of nasopharyngeal carcinoma and is the triangular region originally described by Ho. It is defined by three points: (1) the superior margin of the sternal end of the clavicle; (2) the superior margin of the lateral end of the clavicle; and (3) the point where the neck meets the shoulder. Note that this would include caudal portions of levels IV and VB. All cases with lymph nodes (whole or part) in the fossa are considered N3b.

Nasopharynx Treatment Guidelines:

5 a. Early cancers, T1 N0 (Stage 1):

- Radical RT (IMRT)

5 b. Early cancers, T1N1, T2 N0 (bulky primary or node +):

- Radical RT (IMRT) +/- chemo
- Radical RT (IMRT) if not fit/suitable for Concurrent treatment

5 c. Advanced cancers, T3, T4 N+ M0:

- Chemoradiotherapy followed by 3 cycles of Chemotherapy or Induction Chemotherapy followed by CRT
- RT alone if not suitable or fit for Concurrent treatment.

5 d. M1 disease: Systemic chemotherapy plus or minus RT for palliation

6. Ethmoid Tumours Treatment:

(Possible Histology: Squamous cell carcinoma, Adenocarcinoma, *SNUC, *SNEC, Minor Salivary Gland Carcinoma/Tumour, Esthesioneuroblastoma, Lymphoma, melanoma and Sarcoma)

6a. Early Tumours (T1, T2):

- Surgical Resection followed by PORT or Surgery and Observation for T1 tumours. If adverse features for CRT.
- RT alone

6b. Advanced Tumours (T3, T4a):

- Surgical Resection followed by PORT/CRT or
- CRT/RT or Induction Chemotherapy followed by CRT/RT

6c. Very Advanced Tumours (T4b and/or M1) or Patient Declines Surgery:

- CRT or RT
- Systemic chemotherapy followed by CRT/RT

6d. Diagnosed after polypectomy:

- Gross Residual disease: Surgery or CRT or RT
- No residual disease: RT or Surgery

* For SNUC (Sino nasal undifferentiated carcinoma and SNEC (Small cell or Sino nasal neuroendocrine carcinomas) histologies systemic therapy should be part of the overall treatment.

Nasal Cavity and Ethmoid Sinus (T staging)

T1 Tumour restricted to any one subsite, with or without bony invasion

T2 Tumour invading two subsites in a single region or extending to involve an adjacent region within the nasoethmoidal complex, with or without bony invasion

T3 Tumour extends to invade the medial wall or floor of the orbit, maxillary sinus, palate, or cribriform plate

T4a Moderately advanced local disease: Tumour invades any of the following: anterior orbital contents, skin of nose or cheek, minimal extension to anterior cranial fossa, pterygoid plates, sphenoid or frontal sinuses

T4b Very advanced local disease: Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than (V2), nasopharynx or clivus.

N staging: same as other tumour subsites.

7. Maxillary Tumours:

(Possible Histology: Squamous cell carcinoma, Adenocarcinoma, *SNUC, *SNEC, Minor Salivary Gland Carcinoma/Tumour, Esthesioneuroblastoma [likely to involve Ethmoids], Lymphoma, melanoma and Sarcoma)

Treatment Recommendations:

7a. Early Tumours:

- 7a 1. T1, T2 N0: Surgery (post op RT/CRT if risk factors)
- 7a 2. T1, T2 N0: (Adenoid cystic carcinoma)
Supra-structure tumours (Above 'Ohngren's' line)
Surgery plus RT
Infra-structure tumours (Below 'Ohngren's' line)
Surgery and observation vs. RT

7b. Advanced Tumours:

- 7b 1. T3-T4a, N0: Surgery plus post op RT/CRT
- 7b 2. T1-T4a, N+: Surgery + ND plus RT/CRT

7c. Very Advanced Tumours:

- 7c 1. T4b any N M0: Systemic chemotherapy, CRT, RT
- 7c 2. Any T, Any N, M1: Systemic chemotherapy plus or minus RT for palliation

* For SNUC (Sino nasal undifferentiated carcinoma and SNEC (Small cell or Sino nasal neuroendocrine carcinomas) histologies systemic therapy should be part of the overall treatment.

Maxillary Sinus (T staging):

- T1** Tumour limited to maxillary sinus mucosa with no erosion or destruction of bone
- T2** Tumour causing bone erosion or destruction including extension into the hard palate and/or middle nasal meatus, except extension to posterior wall of maxillary sinus and pterygoid plates
- T3** Tumour invades any of the following: bone of the posterior wall of maxillary sinus, subcutaneous tissues, floor or medial wall of orbit, pterygoid fossa, ethmoid sinuses
- T4a** Moderately advanced local disease
Tumour invades anterior orbital contents, skin of cheek, pterygoid plates, infratemporal fossa, cribriform plate, sphenoid or frontal sinuses
- T4b** Very advanced local disease
Tumour invades any of the following: orbital apex, dura, brain, middle cranial fossa, cranial nerves other than V2, nasopharynx or clivus

N staging: same as other tumour subsites.

8. Neck nodes with Unknown Primary:

History and Clinical examination and Fiber-optic scope of UAT and Examination of skin of H&N and Scalp
FNA of neck lump

8a. FNA (With no clear primary in UAT):

Squamous cell carcinoma, Adenocarcinoma (Rarely Prostatic adenocarcinoma, Carcinoid/NET (Neuroendocrine Tumours) may be encountered in ND samples)
Undifferentiated/anaplastic carcinoma.

Work Up:

- PET/CT and MRI (Before EUA and Biopsies)
- Histologic/Cytologic subtypes and immunocyto/histochemistry may help direct further investigations and referral to relevant MDTs. (E.g. with NET/Carcinoid histology: CT/MRI Chest/abdomen, Tumour markers (Chromogranins A & B, 24 hour Urine 5 HIAA), Octreoscan etc. In Prostatic adenocarcinoma: PSA and Pelvic MRI)
- HPV and EBV testing on histology and immunostaining (e.g. TTF1, CK 7, 20, PSA, hormone receptor status can be crucial in guiding further investigations)
- Thyroglobulins, Calcitonins if FNA suggestive of thyroid cancer

Node levels 1, 2, 3, Upper 5:

- EUA, biopsies of areas of concern, or biopsies of BOT, Piriform fossa, Nasopharynx and Bilateral Tonsillectomies.

Node Levels Lower 5 and 4:

- Evaluate for Infraclavicular primary, especially in Adenocarcinomas. In Adenocarcinoma, in non-smokers assess for EGFR and ALK mutations of Biopsies. OGD and other investigations based on immunocyto(histo)chemistry.

Treatment Recommendations:

8a 1. Primary Identified: Treat as per guidance for the respective primary cancers

8a 2. No Primary Identified:

- Neck dissection or CRT
- Total mucosal irradiation can be considered. CRT to neck and oropharynx preferred if HPV+ve.
- Node with ECS, HPV-ve: Neck dissection preferred.
- Elderly patients / unfit for concurrent chemotherapy: Neck Dissection
- Adjuvant chemoradiotherapy or RT depending on risk factors (e.g. ECS, multiple nodes, PNI, VI)

8b. Other Histologies:

Lymphoma, Thyroid cancers, Melanomas, Sarcomas

Refer to relevant MDT/Guidelines: if Adenocarcinoma/Squamous carcinoma with an occult primary likely to be in non-head and neck locations: Refer to CUP oncology team

Treatment Algorithm post ND in Unknown Primary:

N1 with No ECS:

- Observation Vs. RT (Target volume dependent on node size, location, HPV and EBV status)

N2, N3 with No ECS:

- RT vs. CRT (Target volume dependent on node size, location, HPV and EBV status)

Any N with ECS:

- CRT

9. Major Salivary Gland Tumours:

Usually patients with parotid cancers are discussed in MDT before any resection is undertaken. However, in some instances a resection has already been undertaken on the basis of pre-operative assessments suggesting a benign pathology.

Rare Histologies: High Grade Salivary carcinoma (often Her 2 +ve), an aggressive pathology with high risk for recurrence and metastases. Mammary analogue secretory carcinoma (MASC, with ETV6 translocation), Merkel cell carcinoma (origin could be in adjacent skin, very highly malignant with risk for recurrence and metastases) Soft tissue sarcomas (E.g. Rhabdomyosarcoma).

Ki 67 index and resection margins can help ascertain the need for adjuvant therapy.

Work Up:

CT/MRI H&N

CT chest

US Neck

Obtain Tissue Diagnosis

Treatment Recommendations:

9a. T1, T2: Aim for complete (re) excision:

- Benign, completely excised: No RT
- Benign but tumour spillage suspected (incomplete excision): RT
- Low Grade carcinoma: RT vs. Observation
- Adenoid Cystic, Other Histologies with Intermediate or High Grade tumours: RT

9b. T3, T4 a N0/N+: Surgery to Primary +/- ND

- Complete excision and no adverse factors: FU
- Adenoid Cystic carcinoma: Post OP RT
- If Adverse factors (Intermediate or High Grade, Close or Positive Margins, PNI, NI, VI, LVI, N+) present: PORT or CRT
- If incomplete excision or Residual disease: Consider re-resection if possible before RT/CRT

9c. T4b: No surgical resection possible or surgery not recommended:

- RT/CRT

9d. Recurrent and Metastatic disease

- PS 0 – 2: Consider re-resection if feasible, Systemic chemotherapy, Expectant management for slow growing tumours, Selected metastasectomy
- Adjuvant RT after resection if no previous RT.
- Irresectable: RT/CRT
- PS 3: BSC

9e. Neck Dissection:

If N +: ND recommended.

In Parotid Tumours: ND if high T stage or high grade histology in N0 neck

TNM Staging System for the Major Salivary Glands (Parotid, Submandibular, and Sublingual)

T1: Tumour 2 cm or less in greatest dimension without extraparenchymal extension*

T2: Tumour more than 2 cm but not more than 4 cm in greatest dimension without extraparenchymal extension*

T3: Tumour more than 4 cm and/or tumour having extraparenchymal extension*

T4a: Moderately advanced disease

Tumour invades skin, mandible, ear canal, and/or facial nerve

T4b: Very advanced disease

Tumour invades skull base and/or pterygoid plates and/or encases carotid artery

*Note: Extraparenchymal extension is clinical or macroscopic evidence of invasion of soft tissues. Microscopic evidence alone does not constitute extraparenchymal extension for classification purposes

Nodal staging: Similar to other HN cancers.

10. Mucosal Melanoma:

Mucosal melanomas of head and neck can often be found in the eyes, mouth, nasal cavity, nasopharynx and larynx. They make up approximately 1.1% of all melanomas. They are often diagnosed late due to their less visible locations and because they are sometimes amelanotic in these locations.

Examine HN, Skin, and UAT Scope.
Verify Immunocyto/histochemistry: HMB-45, S-100, Melan-A.
MRI HN, CT chest, Consider PET/CT.
BRAF testing recommended for all stage 4 patients

Treatment Recommendations:

10 a. Sino-Nasal MM:

Stage 3:	Surgical Resection and Consider RT
Stage 4a (T4 a N0):	Surgery Plus RT
Stage 4 a (N +):	Surgery to Primary and ND Plus RT
Stage 4 b:	Clinical Trial, RT, Systemic Therapy. (Liaise with/Refer to Medical oncologist)
Stage 4 c:	Clinical Trial, RT, Systemic Therapy, BSC. (Liaise with/Refer to Medical oncologist)

10 b. Oral, Pharynx, Larynx MM:

Stage 3:	Surgical excision Plus Elective ND, Strongly consider RT
Stage 4 a:	Surgical excision, ND, Plus RT
Stage 4 b:	Clinical Trial, RT, Systemic Therapy. (Liaise with/Refer to Medical oncologist)
Stage 4 c:	Clinical Trial, RT, Systemic Therapy, BSC. (Liaise with/Refer to Medical oncologist)

Node positive MM, Occult Primary: ND, Parotidectomy (if indicated) plus PORT.

TNM Staging System for Mucosal Melanoma of the Head and Neck

(Stage starts at T3)

T3 Mucosal disease

T4a Moderately advanced disease Tumour involving deep soft tissue, cartilage, bone, or overlying skin

T4b Very advanced disease Tumour involving brain, dura, skull base, lower cranial nerves (IX, X, XI, XII), masticator space, carotid artery, prevertebral space, or mediastinal structures

NX: Regional lymph nodes cannot be assessed
N0: No regional lymph node metastases
N1: Regional lymph node metastases present

Stage III: T3 N0 M0
Stage IVA: T4a N0 M0; T3-T4a, N1 M0
Stage IVB: T4b, Any N, M0
Stage IVC: Any T, Any N, M1

11. Head and Neck Sarcoma:

(See Appendix 4 for more information on staging, subtypes and Management guidelines)

Sarcomas account for < 1% of malignant neoplasm in the Head and Neck. (20% from bones and cartilages and 80% in soft tissues) The most frequent histology is Malignant fibrous histiocytoma (MFH – 29%), the least common is Liposarcoma (1%). Other histologies include Osteosarcoma, Ewing Sarcoma, Kaposi Sarcoma, Fibrosarcoma, Angiosarcoma, leiomyosarcoma, Alveolar soft part sarcoma, Chondrosarcoma, Malignant Schwannoma, Neurofibrosarcoma, Rhabdomyosarcoma and Synovial sarcomas. Histologic assessments by immunocytochemistry and chromosomal translocation characterisation may be necessary for diagnosis. Radiation induced sarcoma (RIS) is a rare late complication of radiotherapy, often with a latent period of 10 years or more.

Surgery remains the mainstay of treatment. Radical surgery followed by postoperative RT is often recommended.

The staging system is the same as for sarcomas of the limbs, although specific staging for Head and Neck Sarcomas is not standardised.

Discussion with and early referral to Sarcoma MDT/ Sarcoma Oncologist is recommended. Sarcoma MDT is hosted from Liverpool. A proforma needs to be completed and it is recommended that histology samples be sent to the Sarcoma Specialist Histopathologist at Aintree hospital in all cases.

Treatment Recommendations:

11 a. Localised (Resectable) Tumour (non-metastatic):

- Surgical Resection followed by postoperative radiotherapy.
- Pre-operative Radiotherapy (50 Gray in 20 fractions over 5 weeks) followed by (4-6 weeks later) surgery. (Routine enteral feeding is not recommended unless there is a significant pre-existing nutritional issue).

Combination surgery and radiotherapy (RT) is frequently used in soft tissue sarcoma (STS). Because lower doses and smaller irradiation volumes are possible in preoperative RT (pre-op RT), this approach can be especially valuable in anatomic settings where critical organs are in close proximity to the RT target area such as Head and Neck Subsites.

Although there is concern regarding increased risk post-operative wound complication after pre-operative RT in Limb (extremity) sarcomas, this has not been shown to be significant in Head and Neck Sarcomas.

11 b. Localised (Resectable) Tumour with Low volume (resectable) metastases:

Discuss with Sarcoma MDT regarding any systemic chemotherapy prior to locoregional treatment as above (11 a).

Metastasectomy with involvement of the respective MDT (e.g. Lung, HPB etc.).

11 c. Irresectable Localised Tumour:

Radical Radiotherapy: If significant response discuss in MDT regarding surgical resection.

11 d. Metastatic Disease:

Refer to Sarcoma Team/MDT for systemic therapy.

12. Recurrent and other rare head and neck tumours:

12 a. Treatment of Local, regional and metastatic disease/recurrence:

- In selected cases with localised recurrence, surgery (if operable) or re-irradiation can be considered.
- For most patients palliative chemotherapy is the standard option.
- First-line option for fit patients should include the combination of cetuximab with cisplatin or carboplatin plus 5-fluorouracil (PF). It resulted in longer survival than PF alone.
- If patients who are unlikely to tolerate combination chemotherapy, single agent chemotherapy can be considered. Weekly methotrexate may be considered for palliation.
- Taxanes are options as well in this context.
- Cetuximab alone has a favourable toxicity profile with activity that is comparable to methotrexate alone.

12 b. Plasmocytoma:

- The common Head and Neck sites are Maxilla and Mandible. The search for multiple myeloma should include skeletal survey, Bone marrow aspirate, Serum electrophoresis and urine Bence Jones protein testing. Presence of paraprotein does not necessarily imply disseminated myeloma. Primary treatment for Head and neck plasmocytoma is Radiotherapy with chemotherapy added to in extensive tumours. Follow up is recommended as many, if not all, may progress to develop multiple myeloma.

12 c. Paragangliomas/ Carotid Body tumours (Chemodectoma, Glomus tumours):

- Paragangliomas are highly vascular neoplasms arising embryologically from the paraganglia of neural crest origin and occurring most commonly in the head and neck region. Typically, paragangliomas manifest in the 5th or 6th decade of life. More common in women. A slowly enlarging neck mass and/or findings consistent with cranial nerve dysfunction are the hallmarks of presentation. Paraganglia are part of the diffuse neuroendocrine system, previously known as the amine precursor decarboxylate system, and have the potential to secrete neuropeptides and catecholamines. Paragangliomas most commonly occur in the carotid body, jugulotympanic area and vagal paraganglia. Rarely these seen in other head and neck subsites. Multi-centric tumors are common in familial cases. Malignant paragangliomas are uncommon. Cranial neuropathy is frequent with 8th, 9th and 10th nerve involvement with tympanojugulare tumours and 10th and 11th for vagale tumours. Other cranial nerve palsies reported are 5th, 6th and 7th with skull base involvement. CT and MRI and Angiogram are essential in planning treatment. MIBG or Octreoscan scans can be useful. Surgery has been the preferred method of treatment, although XRT is an option in those whom (elderly, less fit patients or with locally advanced tumours) resection would produce unacceptable morbidity. Pre-operative embolisation is beneficial. Radiation doses of 50-55 Gy in 25 fractions are recommended .

12 d. Chordoma:

Chordomas originate in the axial skeleton from the remnants of primitive notochord. About 50% arise in the sacrococcygeal area; 35% intracranially, typically involving Clivus; remaining in the midline structures such as cervical vertebrae. CT and MRI scans are necessary. Metastases can occur to Lung, Liver and bone. The surgical inaccessibility, proximity to critical organs and the relative radio-resistance (requiring higher doses of radiation) represent a therapeutic challenge. Surgical resection is recommended if feasible. Post-operative radiotherapy is often needed. Radical radiotherapy and Proton therapy are options in irresectable tumours.

12 e. Juvenile angiofibroma:

Tumour affects adolescent males and present with nasal obstruction, facial deformity and/or epistaxis. It is benign but may behave in a malignant fashion. CT, MRI and Angiogram are recommended. Pre-operative embolization can be done. Surgery is the treatment of choice. XRT is an option in irresectable, recurrent tumours. Doses of 30 Gy in 15-22 fractions are sufficient.

12 f. Esthesioneuroblastoma (Olfactory neuroblastoma):

This small round blue cell tumours arise from the roof of the nose. Presenting symptoms are nasal obstruction, anosmia, nasal discharge and epistaxis. Proptosis and diplopia can result from orbital invasion.

The Kadish system used for staging as follows.

- A. Confined to nasal cavity
- B. Involvement of paranasal sinuses
- C. Spread beyond nasal cavity and paranasal sinuses.

Surgical resection is the primary treatment. These are radiosensitive tumours and post-operative radiotherapy should be considered in high-grade tumours with close or involved excision margins. The doses used are 50 Gy in 20 fractions. In irresectable or inoperable tumours, doses of 55 Gy in 20 or the equivalent are necessary. Distant metastases can occur. Chemotherapeutic regimen such as CAV and Platinum based regimens can be used.

12 g. Tumours of External and Middle ear:

Squamous cancers of the middle ear are very rare; there is an association with chronic suppurative ear disease. CT and MRI are essential for staging.

Stell Staging:

- T1. Tumour limited to site of origin with no facial nerve palsy or bone erosion
- T2. Extends beyond site of origin to involve bone and cause facial palsy
- T3. Extension to surrounding structures, dura, skull base, parotid gland, TMJ etc.

Treatment is combination of conservative resection and post-operative radiotherapy. XRT doses used are 50 Gy in 20 fractions and some early tumours may be treated with XRT alone with doses of 52-55 Gy in 20 fractions.

Tumours of External auditory canal: Stell staging can be used. CT and MRI are necessary for staging. Surgery followed by Post-operative radiotherapy is recommended.

Tumours of Pinna: Majority are squamous cancers of the skin and may be treated with XRT or Surgery

12 h. Merkel cell carcinoma:

These are aggressive malignant tumours of the dermis of the skin that resemble small cell carcinomas of the lung. These have a tendency to spread and metastasize. It affects the elderly and often has a short history. Surgical resection plus or minus ND and post-operative XRT is recommended. XRT alone with or without Chemotherapy with CAV/EP regimens can be used.

13. Head and Neck Chemotherapy Treatment Algorithms

Neo-adjuvant treatment

- 2 - 3 cycles of TPF* if PS 0 or 1
- 2 to 3 cycles of PF* if PS 0-2 and other comorbidities

Concomitant chemoradiotherapy for locally advanced head and neck cancer

- weekly Cisplatin (30-40 mg/m²/week) 6 cycles or;
- Fractionated Cisplatin 50 mg/m² (D1 and D2 and then D25 and D26)
- Cisplatin 100 mg /m² D1 and D29 or Carboplatin AUC 5 D1 and D29
- weekly Carboplatin (AUC 1.5 - 2) 6 cycles
- weekly Cetuximab 6 cycles if platinum is contraindicated

Palliative treatment

- Platinum 5FU up to 6 cycles (with Cetuximab if PS 0/1). Maintenance Cetuximab if stable disease or continued response until progression or development of toxicities
- Platinum and Gemcitabine (Nasopharynx)
- Platinum plus Taxanes*
- 2nd line: Docetaxel 75 mg / m² q21
- Single Agent Platinum, Methotrexate, Gemcitabine (Nasopharynx).

* TPF = Taxotere (Docetaxel), Platinum (Cisplatin or Carboplatin) and 5 FU.

* PF = Platinum (Cisplatin or Carboplatin) and 5 FU.

* Taxanes = Docetaxel or Paclitaxel

Appendix 1:

Adult Co-morbidity Evaluation (ACE-27) UK Values

The following form was developed as an extract from the National Cancer Dataset v4.0. We acknowledge that the intellectual property rights remain with Washington University in St. Louis, Campus Box 8013, 660 So. Euclid Avenue, St Louis MO 63110. It originates from and was developed with the permission of Washington University in St Louis.

Cogent comorbid ailment	Grade 3 Severe Decompensation	Grade 2 Moderate Decompensation	Grade 1 Mild Decompensation
Cardiovascular System			
Myocardial Infarct	<ul style="list-style-type: none"> MI \leq 6 months 	<ul style="list-style-type: none"> MI > 6 months ago 	<ul style="list-style-type: none"> Old MI by ECG only, age undetermined
Angina / Coronary Artery Disease	<ul style="list-style-type: none"> Unstable angina 	<ul style="list-style-type: none"> Chronic exertional angina Recent (\leq 6 months) Coronary Artery Bypass Graft (CABG) or Percutaneous Transluminal Coronary Angioplasty (PTCA) Recent (\leq 6 months) coronary stent 	<ul style="list-style-type: none"> ECG or stress test evidence or catheterization evidence of coronary disease without symptoms Angina pectoris not requiring hospitalization CABG or PTCA (>6 mos.) Coronary stent (>6 mos.)
Congestive Heart Failure (CHF)	<ul style="list-style-type: none"> Hospitalized for CHF within past 6 months Ejection fraction < 20 per cent 	<ul style="list-style-type: none"> Hospitalized for CHF >6 months prior CHF with dyspnea which limits activities 	<ul style="list-style-type: none"> CHF with dyspnea which has responded to treatment Exertional dyspnea Paroxysmal Nocturnal Dyspnea (PND)
Arrhythmias	<ul style="list-style-type: none"> Ventricular arrhythmia \leq 6 months 	<ul style="list-style-type: none"> Ventricular arrhythmia > 6 months Chronic atrial fibrillation or flutter Pacemaker 	<ul style="list-style-type: none"> Sick Sinus Syndrome
Hypertension	<ul style="list-style-type: none"> DBP > 130 mm Hg Severe malignant papilledema or other eye changes Encephalopathy 	<ul style="list-style-type: none"> DBP 115-129 mm Hg DBP 90-114 mm Hg while taking antihypertensive medications Secondary cardiovascular symptoms: vertigo, epistaxis, headaches 	<ul style="list-style-type: none"> DBP 90-114 mm Hg while not taking antihypertensive medications DBP < 90 mm Hg while taking antihypertensive medications Hypertension, not otherwise specified
Venous Disease	<ul style="list-style-type: none"> Recent PE (\leq 6 mos.) Use of venous filter for PE's 	<ul style="list-style-type: none"> DVT controlled with Coumadin or heparin Old PE > 6 months 	<ul style="list-style-type: none"> Old DVT no longer treated with Coumadin or Heparin
Peripheral Arterial Disease	<ul style="list-style-type: none"> Bypass or amputation for gangrene or arterial insufficiency < 6 months ago Untreated thoracic or abdominal aneurysm (>6 cm) 	<ul style="list-style-type: none"> Bypass or amputation for gangrene or arterial insufficiency > 6 months ago Chronic insufficiency 	<ul style="list-style-type: none"> Intermittent claudication Untreated thoracic or abdominal aneurysm (< 6 cm) s/p abdominal or thoracic aortic aneurysm repair
Respiratory System			
	<ul style="list-style-type: none"> Marked pulmonary insufficiency Restrictive Lung Disease or COPD with dyspnea at rest despite treatment Chronic supplemental O₂ CO₂ retention (pCO₂ > 6.7 kPa) Baseline pO₂ < 6.7 kPa FEV₁ (< 50 per cent) 	<ul style="list-style-type: none"> Restrictive Lung Disease or COPD (chronic bronchitis, emphysema, or asthma) with dyspnea which limits activities FEV₁ (51 per cent-65 per cent) 	<ul style="list-style-type: none"> Restrictive Lung Disease or COPD (chronic bronchitis, emphysema, or asthma) with dyspnea which has responded to treatment FEV₁ (66 per cent-80 per cent)
Gastrointestinal System			
Hepatic	<ul style="list-style-type: none"> Portal hypertension and/or esophageal bleeding \leq 6 mos. (Encephalopathy, Ascites, Jaundice with Total Bilirubin > 34mmol/l) 	<ul style="list-style-type: none"> Chronic hepatitis, cirrhosis, portal hypertension with moderate symptoms "compensated hepatic failure" 	<ul style="list-style-type: none"> Chronic hepatitis or cirrhosis without portal hypertension Acute hepatitis without cirrhosis Chronic liver disease manifested on biopsy or persistently elevated bilirubin (>51mmol/l)
Stomach / Intestine	<ul style="list-style-type: none"> Recent ulcers \leq 6 months requiring \geq 6 units of blood transfusion 	<ul style="list-style-type: none"> Ulcers requiring surgery or transfusion of < 6 units of blood 	<ul style="list-style-type: none"> Diagnosis of ulcers treated with meds Chronic malabsorption syndrome Inflammatory bowel disease (IBD) on meds or h/o with complications and/or surgery
Pancreas	<ul style="list-style-type: none"> Acute or chronic pancreatitis with major complications (phlegmon, abscess, or pseudocyst) 	<ul style="list-style-type: none"> Uncomplicated acute pancreatitis Chronic pancreatitis with minor complications (malabsorption, impaired glucose tolerance, or GI bleeding) 	<ul style="list-style-type: none"> Chronic pancreatitis w/o complications

Appendix 2:

Table 1. Charlson Comorbidity Index Scoring System

Score	Condition
1	Myocardial infarction (history, not ECG changes only) Congestive heart failure Peripheral vascular disease (includes aortic aneurysm ≥ 6 cm) Cerebrovascular disease: CVA with mild or no residua or TIA Dementia Chronic pulmonary disease Connective tissue disease Peptic ulcer disease Mild liver disease (without portal hypertension, includes chronic hepatitis) Diabetes without end-organ damage (excludes diet-controlled alone)
2	Hemiplegia Moderate or severe renal disease Diabetes with end-organ damage (retinopathy, neuropathy, nephropathy, or brittle diabetes) Tumor without metastases (exclude if >5 y from diagnosis) Leukemia (acute or chronic) Lymphoma
3	Moderate or severe liver disease
6	Metastatic solid tumor AIDS (not just HIV positive)

NOTE. For each decade > 40 years of age, a score of 1 is added to the above score.

Abbreviations: ECG, electrocardiogram; CVA, cerebrovascular accident; TIA, transient ischemic attack; AIDS, acquired immunodeficiency syndrome; HIV, human immunodeficiency virus.

Table 2
One and Two-Year Survival Probabilities Across Charlson Comorbidity Index Levels**
Albumin ≤ 3.5 g/dL

CCI Level	n	Frequency*	Probability of 1 year survival (95% confidence interval)	Probability of 2 year survival (Confidence interval)
2-3	34	2%	0.91 (0.81-1.00)	0.87 (0.77-0.99)
4-5	97	6%	0.73 (0.64-0.82)	0.61 (0.49-0.73)
6-7	173	10%	0.69 (0.62-0.77)	0.49 (0.41-0.59)
>8	138	8%	0.52 (0.43-0.61)	0.30 (0.20-0.40)

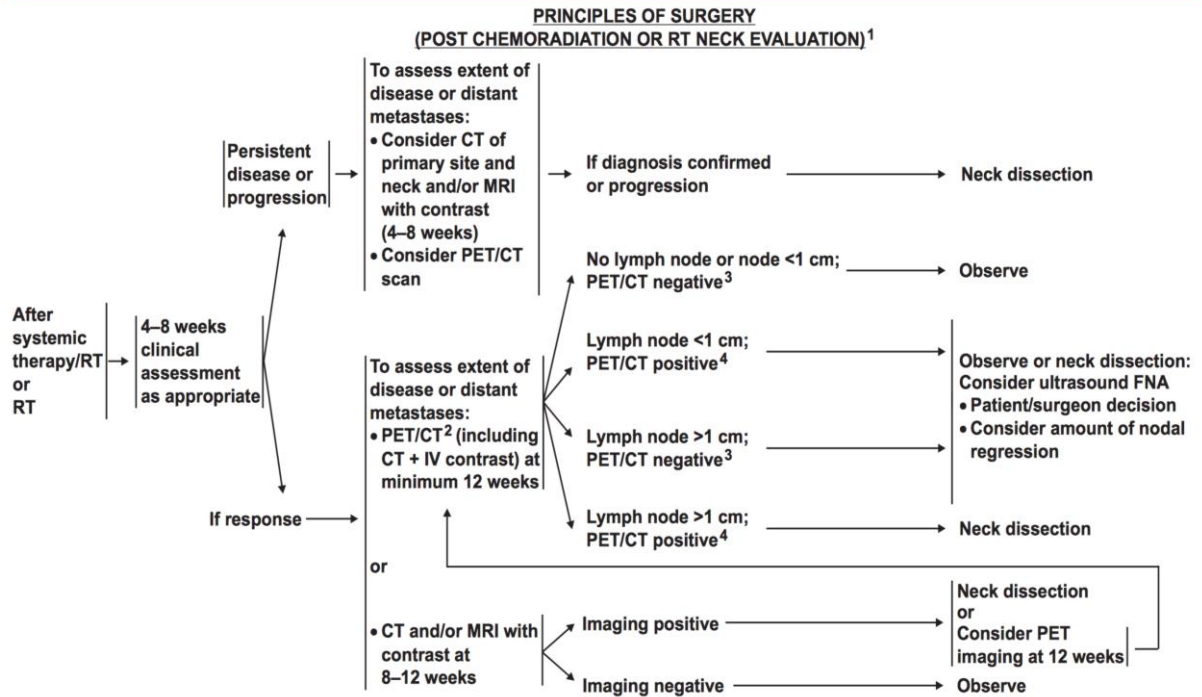
Albumin ≥ 3.5 g/dL CCI

CCI Level	n	Frequency*	Probability of 1 year survival (95% confidence interval)	Probability of 2 year survival (Confidence interval)
2-3	230	13%	0.93 (0.90-0.96)	0.89 (0.84-0.93)
4-5	299	17%	0.89 (0.85-0.92)	0.75 (0.69-0.80)
6-7	488	28%	0.84 (0.80-0.87)	0.67 (0.63-0.72)
>8	302	17%	0.75 (0.70-0.80)	0.52 (0.45-0.58)

*Frequency of subjects within groups divided by CCI Level and serum albumin

** Survival probability estimates are based on observation of 1761 incident and prevalent haemodialysis patients from 41 dialysis facilities of Dialysis Clinic Inc.

Appendix 3:



¹Adapted with permission from Kutler DJ, Patel SG, Shah JP. The role of neck dissection following definitive chemoradiation. *Oncology* 2004;18:993-998.

²If a PET/CT is performed and negative for suspicion of persistent cancer, further cross-sectional imaging is optional.

³PET negative = No or low-grade uptake, felt not suspicious for disease.

⁴PET positive = PET suspicious for disease.

Appendix 4:

Sarcoma TNM, Subtype management guidelines

American Joint Committee on Cancer (AJCC) and International Union Against Cancer (UICC) staging system for soft tissue sarcomas

Primary tumor

Tx - Primary tumor cannot be assessed

T0 - No evidence of primary tumor

T1 - Tumor less than 5 cm in greatest dimension (T1a, superficial; T1b, deep)

T2 - Tumor greater than 5 cm in greatest dimension (T2a, superficial; T2b, deep)

Regional lymph nodes

Nx - Lymph nodes cannot be assessed

N0 - No lymph nodes metastases

N1 - Lymph nodes metastases present

Distant metastases

Mx - Distant metastases cannot be assessed

M0 - No distant metastases

M1 - Distant metastases present

Histopathologic grade

Gx - Grade cannot be assessed

G1 - Well-differentiated

G2 - Moderately differentiated

G3 - Poorly differentiated

G4 - Undifferentiated

Combined

IA (G1-2, T1a-b, N0, M0) - Low-grade, small, and superficial or deep tumor

IB (G1-2, T2a, N0, M0) - Low-grade, large, and superficial tumor

IIA (G1-2, T2b, N0, M0) - Low-grade, large, and deep tumor

IIB (G3-4, T1a-b, N0, M0) - High-grade, small, and superficial or deep tumor

IIC (G3-4, T2a, N0, M0) - High-grade, large, and superficial tumor

III (G3-4, T2b, N0, M0) - High-grade, large, and deep tumor

IV (any G, any T, N1, M0) - Any metastasis

Malignant Fibrous Histiocytomas: Surgery followed by PORT (close or positive margins)

Synovial Sarcoma: Hypopharynx common site in HN. A reciprocal translocation, t (X;18)(p11.2;q11.2), has been identified in monophasic and biphasic synovial sarcoma. Surgical excision combined with postoperative radiation therapy is the primary treatment for synovial sarcoma. Local recurrence rates are 60-90% when surgery is the sole therapy. The addition of adjuvant radiotherapy to surgery reduces the recurrence rates to 28-49%. Doses of at least 65 Gy must be used for any survival advantage. Chemotherapy with ifosfamide compounds appears to be of benefit in the treatment of distant metastases.

Chondrosarcomas: These are the most common type of laryngeal sarcoma and the second most common type of sarcoma arising from bone in the head and neck. Chondrosarcomas are slow growing, locally invasive lesions. Surgical resection is the main treatment for Chondrosarcomas. Chondrosarcomas arising in the larynx are associated with a better prognosis, although total laryngectomy is often required for complete removal. Conservation surgery is associated with a higher incidence of local recurrence. Chondrosarcomas arising in the nasopharynx or sinonasal tract are associated with a poorer prognosis. Chondrosarcomas are considered to be resistant to radiotherapy, and, in general, adjuvant radiation therapy is not used. However, survival rates increase with chondrosarcomas of the base of the skull with postoperative irradiation; this finding suggests that some lesions may be sensitive to radiation therapy. Chemotherapy does not have a demonstrable benefit in the management of chondrosarcoma, but chemotherapy is sometimes used for high-grade tumors with distant metastasis.

Rhabdomyosarcomas: In head and neck, 4 subtypes of rhabdomyosarcoma have been described: embryonal, alveolar, pleomorphic, and mixed. The embryonal subtype is the most common (>70%). Multimodality therapy with combination chemotherapy (vincristine, actinomycin D, cyclophosphamide, Adriamycin) with external-beam radiation therapy and nonradical surgery is superior to any single-modality therapy. Surgery has a smaller role in the treatment of this sarcoma; surgery is performed for biopsy and tumor debulking.

T1 - Tumor confined to organ or tissue of origin

T2 - Tumor involving one or more contiguous organs or tissues

Nx - Lymph nodes cannot be assessed

N0 - No lymph nodes metastases

N1 - Lymph nodes metastases present

Mx - Distant metastases cannot be assessed

M0 - No distant metastases

M1 - Distant metastases present

Malignant Schwannomas: Also known as malignant peripheral nerve sheath tumors or neurofibrosarcomas, arise from peripheral or cranial nerves. Malignant schwannomas may arise sporadically or in association with von Recklinghausen disease or neurofibromatosis type I (NF-1). The most common site of origin in the head and neck is the neck, followed by the nasal cavity and paranasal sinuses, nasopharynx, oral cavity, orbit, cranial nerves, and larynx. Management of malignant schwannoma is primarily surgical; adjuvant radiation therapy is often used because most of these tumors are high-grade.

Liposarcomas: Typically, liposarcomas are slow growing, painless masses. With the exception of lesions in the larynx, which can cause dysphagia and airway symptoms, most patients with liposarcomas are asymptomatic at presentation. Wide local excision is the treatment of choice for liposarcomas; wide margins are especially important for local control, given the degree of infiltration associated with these tumors despite their apparent capsules. The role of radiation therapy in the treatment of liposarcomas is a subject of continued debate, although liposarcomas, particularly the well-differentiated and myxoid subtypes, are sensitive to radiation therapy. Radiotherapy is suggested as an alternative to surgery in lesions in which surgical resection would cause significant and unacceptable cosmetic or functional defect and in the postoperative setting after incomplete tumor resection.

Alveolar soft part sarcoma: Surgical excision is the treatment of choice. Adjuvant radiotherapy or chemotherapy has not been shown to provide any improvement in disease control or survival.

Kaposi's sarcoma: Treatment for KS is non-surgical and consists of either radiotherapy (XRT) or chemotherapy. The choice of treatment is based on the extent of disease.

Osteosarcoma: The mandible and maxilla are the most frequently affected sites, followed by the paranasal sinuses and skull. Surgical excision is the main treatment for osteosarcoma. Adjuvant radiation therapy has been used in the management of osteosarcoma when wide surgical margins cannot be obtained; however, osteosarcomas are relatively resistant to radiation therapy, and doses in excess of 6000 Gy are required. The use of neoadjuvant chemotherapy (cisplatin, doxorubicin) appears to be of benefit in some patients.

Ewing sarcoma: Multimodality therapy for Ewing sarcoma is associated with markedly improved survival rates. Surgery followed by adjuvant XRT and multi-agent chemotherapy dramatically improves survival rates, compared with single- or even dual-modality therapy. Complete surgical excision is undertaken whenever possible. XRT may be withheld when complete surgical excision can be accomplished with clear margins. The use of adjuvant XRT is associated with improved local control because it treats microscopic residual disease. Multi-agent chemotherapy has dramatically improved the 5-year survival rates from 10% prior to its use to 50-75% today. Ifosfamide with etoposide or vincristine, dactinomycin, and cyclophosphamide are most commonly used.