CANCERS OF THE HEAD AND NECK
PREFERRED MODEL OF CARE AND CRITERIA FOR REFERENCE CENTRES
Coordinator: Marc Hamoir (Otolaryngology, Head & neck surgery, Cliniques universitaires St Luc)

Authors: Marc Hamoir (Otolaryngology, Head & neck surgery, Cliniques universitaires St Luc), Johan Abeloos (MKA Maxillofacial surgery, AZ St Jan Brugge), Guy Andry (Head and neck surgery, Institut Jules Bordet ULB), Philippe Deron (Otolaryngology, Head and neck surgery, UZ Gent), Frédéric Duprez (Radiotherapy, UZ Gent), Olivier Lenssens (MKA Oral & maxillofacial surgery, ZNA Middelheim), Max Lonneux (Nuclear medicine, CHIREC E. Cavell, Bruxelles), Etienne Marbaix (Pathology, Cliniques universitaires St Luc), Jean-Pascal Machiels (Medical Oncology, Cliniques universitaires St Luc), Sandra Nuyts (Radiotherapy Oncology, UZ Leuven), Carl Van Laer (Otolaryngology-Head & neck surgery, UZA), Vincent Vander Poorten (ORL Head & neck surgery, UZ Leuven), Jan Vermorken (Medical Oncology, UZA), Birgit Weynand (Pathology, CHU Mont Godinne), Vincent Grégoire (Radiotherapy-oncology, Cliniques universitaires St Luc)

Disclaimer:
- The coordinators of the working groups and all the authors listed by chapter have worked autonomously under the supervision of the KCE team. The KCE experts are not co-authors of these proposals and did not necessarily validate their content.
- Hospitals with which coordinators and authors of these proposals are affiliated are not de facto considered Reference Centres. Similarly, Belgian hospitals that are not represented in these proposals are not de facto considered Peripheral Centres.
- These proposals were not submitted to the external validators.
- This addendum only exists in English. No French or Dutch translation was done.
- Finally, the report to which this addendum refers has been approved by common assent by the Executive Board.

Copyright: KCE reports are published under a “by/nc/nd” Creative Commons Licence http://kce.fgov.be/content/about-copyrights-for-kce-reports.

This section is part of a whole document (KCE Report 219 Addendum) available on the website of the Belgian Health Care Knowledge Centre
A. Sub-localisations of head & neck cancer
Oral cavity, oropharynx, larynx, hypopharynx, nasopharynx, nasal cavity & paranasal sinus, middle ear, skull base, salivary glands

B. Short description of head & neck cancer

Head and neck cancer refers to a group of biologically diverse cancers that start in the Upper Aerodigestive Tract (UAT), including oral cavity, larynx, oropharynx, hypopharynx, and very rare tumours arising in nasal cavity and paranasal sinus, nasopharynx, middle ear, salivary glands and skull base. In addition to those tumours, managed by a head & neck multidisciplinary team, thyroid gland cancer, sarcomas of the head and neck and advanced skin cancer adjacent to the ear or the nose are frequently managed by the same team. Mean age at diagnosis is 62 years in males and 63 years in females. The majority of head and neck cancers of the upper aerodigestive tract is squamous cell carcinomas (SCC) and is associated with a history of smoking and alcohol use. This is not the case for cancers of the paranasal sinuses or salivary gland. In addition, tumours of the nose or paranasal sinuses have been linked with occupational and chemical exposures. Infection with human papilloma virus (HPV) is now also accepted as a contributing risk factor for the development of oropharyngeal cancers. Head & neck cancer occurs preferentially in males (male/female ratio in Belgium: 3.7). In 2010, there were 2,395 newly diagnosed head and neck cancers in Belgium. The overall cumulative incidence rate for head & neck cancer is around 21 per 100,000 population. This includes cancers of the oral cavity (682 cases, 6.2 per 100,000 population) and lip (61 cases, 0.6 per 100,000 population), larynx (676 cases, 6.1 per 100,000 population), oropharynx (503 cases, 4.5 per 100,000 population), hypopharynx (219 cases, 2 per 100,000 population), nasopharynx (58 cases, 0.5 per 100,000 population), paranasal sinuses, nasal cavity and middle ear (121 cases, 1.1 per 100,000 population), skull base cancers form a subset of very rare head & neck cancers arising from the paranasal sinuses or adjacent to the temporal bone, and salivary glands (135 cases, 1.2 per 100,000 population).

In Belgium, the 5-year relative survival rate is 50% and 57%, in males and females respectively. Most deaths related to head and neck cancer occur within the first three years after diagnosis (3-year relative survival of 58.7% in males and 63.7% in females). However, beyond the 5-year period, relative survival further decreases to reach about 39.5% in males and 48.1% in females at 10 years after diagnosis. Patients diagnosed with head and neck cancer are at high risk of developing second primary tumours that can impair their chances of survival (especially tobacco and alcohol related cancers in the upper aerodigestive tract).

Clinical stage is of utmost importance to select initial treatment and serve as a prognostic factor for survival. Whereas the 5-year relative survival for early-stage tumours without lymph node invasion (Stage I) is good (82.4% in males and 77.5% in females), more locally and/or regionally advanced disease have a poorer prognosis (5-year relative survival for stage IV: 31% in males and 36% in females).

Cancer of the oral cavity and the lips represents approximately 30% of all cancers of the head & neck. In Belgium, 743 new patients with cancer of the oral cavity and lips (682 cancer of the oral cavity and 61 cancer of the lips) were diagnosed in 2010, i.e. 32% of all cancer of the UAT. Oral cancer has the highest incidence of the head and neck cancers. Like other cancers of the UAT, it is more common in men than in women. Approximately 90% of oral cancers are SCCs arising from the lining of the mouth. The most frequently invaded subsites are the tongue and the floor of the mouth. The most common symptom of oral cavity cancer is a persistent sore or lump on the lip or in the mouth, but there may also be pain and/or a lump in the neck. Other symptoms are a white or red patch on the gums, tongue or lining of the mouth, and unusual bleeding, pain or numbness in the mouth.

As the oral cavity is extremely rich in lymphatics, cancers originating from this region often present with invaded lymph nodes. Occult metastases have been demonstrated in up to 20 – 44% of patients with oral cavity SCCs whose neck is classified N0. In Belgium, the 5-year relative survival is 51.5% for males and 60.1% for females.
Cancer of the hypopharynx represents approximately 7-8% of all cancers of the upper aerodigestive tract. In Belgium, 219 new patients with hypopharyngeal cancers were diagnosed in 2010, i.e. 9% of all cancer of the UAT. Most of them (75%) are localized in the pyriform sinus, whereas the remaining 25% occurred in other hypopharyngeal sites (posterior pharyngeal wall and post cricoid). The male/female (M/F) ratio is 5 in Belgium. Patients are typically 55–70-year old men, heavy smokers and drinkers. Human papilloma virus (HPV) is implicated to a much lower extent than in oropharynx and oral cancers. Swallowing difficulties and ear pain are common symptoms and hoarseness is not uncommon. Hypopharynx cancers often spread to the lymph nodes of the neck, and this is often the first sign of the disease at the time of diagnosis. The management of hypopharyngeal squamous cell carcinoma remains difficult. Most patients have advanced loco-regional disease at the time of diagnosis. When oncologically suitable, treatment selection should favour laryngeal preservation approaches either surgically or non-surgically to improve the quality of life without compromising locoregional control and survival. Advanced hypopharyngeal cancers have still a dismal prognosis. The frequency of distant metastases is the highest of all subsites of head and neck cancer. During follow-up, 25% of patients locoregionally controlled will develop distant metastases, mainly in the lungs and, to a lower extent, to the liver and the bones. Despite a good local control rate, most patients succumb to distant metastases, intercurrent diseases, or second primaries. Overall 5-year survival rate is approximately 30%. When the 5-year survival rate with early lesions is about 50–60%, in advanced stage, survival drops to 25–35% at 5 years.

Cancer of the nasopharynx: in Belgium, 58 new patients with nasopharyngeal cancers were diagnosed in 2010, i.e. 2.5% of all head and neck cancer. Nasopharynx cancer (NPC) occurs in children and adults and is most common in males. It differs significantly from other cancers of the head and neck in its occurrence, causes, clinical behaviour, and treatment. NPC is uncommon in Belgium and European countries, representing less than 1 case per 100 000 in most populations. The World Health Organization classifies nasopharyngeal carcinoma in three types. Type 1 (I) is squamous cell carcinoma. Type 2a (II) is keratinizing undifferentiated carcinoma. Type 2b (III) is nonkeratinizing undifferentiated carcinoma (WHO Classification. Head and Neck Tumors, 2005). Type 2b (III) nonkeratinizing undifferentiated form also known as lymphoepithelioma is most common, and is most strongly associated with EBV infection of the cancerous cells. Most nasopharyngeal cancer is treated by radiotherapy alone or a combination of chemotherapy and radiotherapy. Early disease limited to nasopharynx can be cured in large majority. Patients with more advanced disease have a higher risk to develop distant metastases during the first years following treatment. In Belgium, the 5-year relative survival is 60% for males and 72.9% for females.

Cancer of the nasal cavity, middle ear and paranasal sinus: in 2010, 121 cases of nasal cavity, middle ear (42 cases) and accessory paranasal sinus (79 cases) were diagnosed in Belgium, i.e. together 5.2% of all head and neck cancer. The 5-year relative survival of patients with cancer of the nasal cavity/middle ear is 64% for males and 53.4% for females. The 5-year relative survival of patients with cancer of the accessory sinuses is 53.1% for males and 37.8% for females.

Cancer of the skull base: Cancers invading the skull base form a subset of rare head and neck cancers. Skull base cancers either arise from the accessory sinuses (anterior skull base) or originate in adjacent soft tissue adjacent to extend into the temporal bone (lateral skull base). The incidence of skull base cancers in Belgium is not known. Because most of those arise from the paranasal sinuses or are adjacent to the middle ear, the number of skull base cancers is obviously included in the overall number of those cancers.
Cancers of the salivary glands: In Belgium, 135 new patients with cancer of the salivary glands were diagnosed in 2010, i.e. 5.8% of all cancer of the head & neck. They comprise a group of more than 35 morphologically different neoplasms with various natural courses requiring specific treatment approaches depending on the pathology. Salivary neoplasms are typically divided into two groups: those arising in the major salivary glands (parotid, submandibular and sublingual gland) and those arising in the minor salivary glands lining the oral cavity, the pharynx, the larynx, the nasal cavity and the paranasal sinuses. Most of them occur in the parotid gland. Surgery is the mainstay of treatment for salivary gland tumors. The difficulty in achieving a proper diagnosis by clinical and radiological parameters implies that surgical removal should be performed with adequate margins. Adjuvant external radiation is indicated for malignant tumors with high-risk features. Because not infrequently, salivary gland tumors are diagnosed as cancer only after surgery, some patients may undergo surgical excision by surgeons not familiar with the management of salivary gland cancers. The prognosis in females is better than in males with a 5-year relative survival of 71.3% and 59.4%, respectively.

C. Model of care pathway suggested for adult patients with head and neck cancers

<table>
<thead>
<tr>
<th>Model of care pathway</th>
<th>Preferred model</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Model 1: Reference Centres exclusively (from diagnosis to follow-up). Once there is a strong suspicion (based on physical examination including fibre optic examination) of one of the cancer type described in A or the cancer type described in A has been diagnosed, the patient should be referred to a Reference Centre. A network with other Reference centres or with specific experts working in other centres is encouraged.</td>
<td></td>
</tr>
<tr>
<td>2. Model 2: Shared care between Reference Centres and peripheral hospitals. Part of the care pathway is performed in the Reference Centre and for another part of the care pathway, the patient is referred (back) to the regional hospital</td>
<td></td>
</tr>
<tr>
<td>3. Model 3: Alternative proposed by the working group. When the diagnosis is suspected, based on physical examination including fibre optic examination, a specific expert working in a peripheral centre is allowed to ask for specific imaging and/or to perform direct endoscopy with biopsy for diagnostic confirmation before referral to the Reference Centre. These examinations need to be performed with the same quality as required in Reference Centres (e.g. drawings and pictures of the tumour during endoscopy, pathologic report, MRI with diffusion-weighted imaging, CT with contrast injection and narrow slices of 1-2mm, Whole-body PET-CT + dedicated H&amp;N sequences (full-resolution, arms along the body, head fixed + contrast-enhanced CT). If not properly performed, these examinations will have to be repeated in the Reference Centres with additional cost and loss of time as consequences. National guidelines for Head and Neck cancer diagnosis procedures need to be published and followed in this field. It should be emphasized that, most of the time, a new endoscopy of the UAT under general anaesthesia will have to be performed in the Reference Centre to evaluate the extent of the tumour, in order to accurately assess the resectability of the tumour, the surgical procedure when surgery is considered or the delineation of the clinical target volume (CTV) if radiotherapy is selected for treatment. Regarding the follow-up, patients may be followed alternatively in the Reference Centre and in the Peripheral Centre</td>
<td>X</td>
</tr>
</tbody>
</table>
D. Phase(s) of the clinical pathway for which Reference Centres are required

<table>
<thead>
<tr>
<th>Phase of the Clinical Pathway</th>
<th>Reference Centre</th>
<th>Peripheral centre</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. COM/MOC</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>2. Diagnostic confirmation</td>
<td>X</td>
<td>X (see model 3)</td>
</tr>
<tr>
<td>3. Comprehensive AP diagnosis</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>4. Therapeutic modalities</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>• Surgery</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>• Radiotherapy</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>• Chemotherapy/Targeted therapy…</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>5. Follow-up</td>
<td>X</td>
<td>X (see model 3)</td>
</tr>
</tbody>
</table>

**Multidisciplinary Oncological Consultation: Reference Centre**

Necessity to gather all the experts involved in specialities dealing with head and neck cancer: diagnosis and treatment. Accurate staging of the tumour. Experience and expertise in management of head & neck cancer.

**Diagnostic confirmation: Reference Centre**

Complexity and new approaches are optimally performed in reference centres by a multidisciplinary team gathering experts (e.g. pathologist, radiologist, nuclear medicine, head & neck surgeons, radiation oncologist, medical oncologist) dedicated to head & neck cancer either exclusively or with a major part of their working time (> 50% FTE for the physicians in charge of the treatment). Together, these experts typically manage a large number of patients per year (minimal number of 100 new cancers of the upper aerodigestive tract (UAT) and salivary glands per year).

**Comprehensive AP diagnosis: Reference Laboratory**

The diagnosis of squamous cell carcinoma (SCC) can be typically performed in most non-reference pathology laboratories. There is however increasing evidence of routine use of immunohistochemistry (for instance: p16 expression,…) and molecular biology in the diagnosis requiring laboratories with adequate facilities and equipment as well as expertise in interpretation of the results. For molecular analysis, reference laboratories exist to which the samples may be referred to. Most of these analyses can be done on formalin fixed paraffin embedded (FFPE) tissue.

Once a patient with a diagnosis of head & neck SCC (performed in a “non reference” laboratory) is referred to a reference centre for work-up completion and treatment, if no additional biopsies need to be performed in the reference centre, upon request from the reference centre, pathology specimens must be sent for revision to the reference laboratory for diagnosis confirmation. Slices and/or blocks should be sent by the non-reference laboratory to the reference centre. Whenever possible, a sample of tumour should be frozen in order to avoid having to redo a biopsy if a non-fixed tumour sample is required.

Every uncommon tumour diagnosis beside classical SCC should be reviewed by an expert from a Reference laboratory. Biobanking should be advised with a sufficient tumour load.
Therapeutic modalities: Reference Centre

- Complexity of treatments: Treatment of head and neck cancer is a very challenging issue. Optimal locoregional control with organ preservation is the main issue. The Reference Centre should propose a panel of treatments aimed to spare organs and preserve function: when oncologically suitable, surgery, radiotherapy alone or combined with chemotherapy or targeted therapies should be favoured. For advanced local disease not suitable for nonsurgical approaches, the surgical team must be able to perform extended resection (e.g. transmandibular oropharyngectomy +/- mandibular bone resection, total laryngopharyngectomy +/- oesophagectomy) and reconstruction using distant pedicled flaps, microvascularized flaps (e.g. mandibular reconstruction using microvascularized composite free flaps, reconstruction of the oesophagus including gastric pull up/colon transposition, after pharyngolaryngectomy and oesophagectomy and speech rehabilitation afterwards). In addition, handling the toxicities caused by the therapy is often challenging. For instance, avoiding treatment interruptions of radiotherapy by good supportive therapy, prevention and management of complications following chemotherapy and targeted therapies to avoid interruptions of treatment or reduction of doses as well as fatal complications.

- Equipment and facilities: Regarding radiotherapy, IMRT or comparable (e.g. rotational therapy) is now a standard in the treatment of head & neck cancers and should be available for head-and-neck cancer in the Reference Centre. Because concomitant chemoradiation is a standard of treatment in many advanced head and cancers, it is obvious that these treatments should be administered in the same institution.

- Expertise required to perform the treatment: Surgery for head and neck cancer requires an expertise in head and neck surgical oncology, conservation surgery, reconstructive surgery and salvage surgery particularly. The selection and delineation of the Gross Tumour Volume (GTV), Clinical Target Volume (CTV) and Organs at Risk (OAR) require a specific expertise in radiation oncology in head & neck cancer as well as the use and knowledge of possible pitfalls of IMRT to treat these patients. A substantial proportion of patients needs combined modality treatment for which cytotoxic or non-cytotoxic medication is required. Integration of this in the whole treatment program in the most optimal manner requires medical expertise having knowledge of the specific needs and limitations of treating such head and neck cancer patients. This overall expertise cannot be maintained if the Centre does not treat at least 100 new cases of cancer of the UAD and salivary glands per year.

- Para-medical expertise required: Clinical nurse specialist (Onco-coach/ CSO specifically dedicated to head & neck cancer patients), nutritionists, dieticians, speech therapists specifically dedicated to head & neck cancer patients, psycho-oncologist specifically dedicated to head & neck cancer patients, nursing staff with specific expertise in the management of head & neck cancer patients (management of postoperative course after major head & neck surgical procedures, management of complications, …)

Follow-up: Reference Centre in collaboration with peripheral centre with a program in oncology

Because the patients are treated in Reference centres exclusively, the follow-up in those same centres is totally justified. According to the expertise of some Peripheral Centres accredited for a program in oncology, an alternated follow-up is a good option and even preferable in patients not living in close proximity of the Reference Centre but only when a specific expert is available in the peripheral centre. Typically, the specific expert is an Otolaryngologist working in a Peripheral Centre and referring the patients to the Reference Centre after diagnosis of the tumour. S/he is able to perform outpatient fibre optic examination of the UAT.

In case of suspicion of recurrence, s/he should inform the Reference Centre immediately. According to the discussion, the patient is sent to the Reference Centre or some procedures (e.g. direct endoscopy, CT, …) are performed in the peripheral centre before referral to the Reference Centre. In any case, evidence of loco-regional recurrence and/or metastatic disease must be demonstrated by biopsy and pathologic confirmation, unless impossibility to sampling tumour tissue but clinical evidence of recurrence/metastasis.
E. General and specific criteria for Reference Centres

Human Resources and dedicated team

The Reference Centre in Head & Neck Cancer is requested to treat a minimum number of new cases of cancer localized in the upper aero-digestive tract (oral cavity, larynx, oropharynx, hypopharynx, nasopharynx, nose and paranasal sinus) and salivary gland cancer per annum. Specifically the Reference Center in head & neck cancer should provide high quality holistic care delivered through a multidisciplinary team, with a special interest in head and neck:

- Surgeons: at least 3 dedicated surgeons, board certified in Otolaryngology, Maxillo-Facial surgery, Head and Neck surgery, or Plastic and Reconstructive surgery. They have a surgical expertise in oncologic surgery for head and neck tumours, including neck dissection, tumour resection by open and transoral approaches, reconstruction by local and distant flaps. At least 1 surgeon in the team should have an expertise in reconstruction with microvascularized flaps (+ 1 back up, when the surgeon with expertise in microvascular surgery is not available). The management of skull base tumours may require the collaboration of 1 surgeon board certified in Neurosurgery, mostly devoted to surgery of brain/skull base tumours (+ 1 back up when the neurosurgeon with specific expertise is not available). Those surgeons should be able to demonstrate an expertise in head and neck surgical oncology, validated by fellowships in head & neck surgical oncology, scientific presentations, publications and presence in head-and-neck oncological symposia. The professional activity of these physicians is exclusively or mostly devoted to head & neck tumours patients (work up, follow-up) and surgery of head & neck tumours.

- Radiation oncologist. At least 1 Radiation Oncologist (+ 1 back up, when the radiation oncologist devoted to H&N cancer is not available) with a special interest in the management of head & neck cancer. All or most of the professional activity of this Radiation Oncologist should be devoted to care of patients with head and neck cancer and s/he should be able to demonstrate an expertise in head and neck radiotherapy, validated by fellowships in head & neck radiotherapy, scientific presentations, abstracts on own data on national or international symposia/meetings, publications and presence in head-and-neck oncological symposia/meetings. When there is only 1 Radiation Oncologist in the multidisciplinary group, one Radiation oncologist member of the department of Radiation Oncology is designated as “back up”, in case of unavailability and should ensure the continuity of care with the same quality level.

- Medical Oncologist. At least 1 Medical Oncologist (+ 1 back up, when the medical oncologist devoted to HN cancer is not available) with a special interest in the management of head & neck cancer. All or most of the professional activity of this Medical Oncologist should be devoted to care of patients with head and neck cancer and she/he should be able to demonstrate an expertise in head and neck oncology, validated by fellowships, scientific presentations, abstracts on own data on national or international symposia/meetings, publications and presence in head-and-neck oncological symposia/meetings. When there is only 1 Medical Oncologist in the multidisciplinary group, one Medical oncologist member of the department of Medical Oncology is designated as “back up”, in case of unavailability and should ensure the continuity of care with the same quality level.

- At least 1 Pathologist with special interest and expertise in patholology of head and neck tumours and expertise in histopathology and cytopathology. When there is only 1 Pathologist in the multidisciplinary group, one Pathologist member of the department of Pathology is designated as “back up”, in case of unavailability and should ensure the continuity of care with the same quality level.

- At least 1 Radiologist with special interest and expertise in imaging of head and neck tumours, combining, at least, expertise in CT, MRI and ultrasonography (US) of the head and neck. When there is only 1 Radiologist in the multidisciplinary group, one Radiologist member of the department of Radiology is designated as “back up”, in case of unavailability and should ensure the continuity of care with the same quality level.
• 1 Nuclear medicine specialist with interest and expertise in PET imaging of head and neck tumours. When there is only 1 Nuclear medicine specialist in the multidisciplinary group, one Nuclear medicine specialist, member of the department of Nuclear medicine, is designated as “back up”, in case of unavailability and should ensure the continuity of care with the same quality level.

• At least 1 oral and maxillofacial surgeon (with 1 back up in case of unavailability), 1 restorative dentist and 1 maxillofacial prosthodontist on-site for the assessment of dental and periodontal status and treatment (restorative and or extractions) before radiotherapy. Proposal of all the ways to avoid osteoradionecrosis. The maxillofacial prosthodontist can help in reconstructive procedures.

• One nutritionist - dietician on-site, with 1 back up in case of unavailability.

• At least one speech therapist on-site specifically dedicated to head & neck cancer patients, with 1 back up in case of unavailability.

• At least one psycho-oncologist on-site specifically dedicated to head & neck cancer patients, with 1 back up in case of unavailability.

• One social worker one-site specifically dedicated to head & neck cancer patients, with 1 back up in case of unavailability.

• Clinical nurse specialist (Onco-coach/ CSO) specifically dedicated to head & neck cancer patients, with 1 back up in case of unavailability.

• Nursing staff with specific expertise in the management of head & neck cancer patients (management of postoperative course after major head & neck surgical procedures, management of complications, …).

Required facilities and equipment

• Radiological, pathological and diagnostic facilities to effectively diagnose, classify and stage the condition prior to planning treatment.

• The accessibility to up-to-date CT, MRI and PET-CT equipment should be guaranteed since they are the core of the initial workup and follow-up of the patients.

• It is of utmost importance to have as participants of the multidisciplinary team the diagnostic radiologist specialists in imaging of head & neck and nuclear medicine physician expert in head & neck tumours to allow a permanent discussion with the members of the group involved in the treatment as imaging require an interpretation according to the input provided by clinicians.

• Pathology department on-site, with daily access for frozen section assessment during surgical procedures.

• Radiotherapy department on the same site or close proximity of the hospital where surgery is performed.

• It is acknowledged that IMRT is currently the standard treatment. It is also acknowledged that when the treatment requires a combination of chemotherapy and radiotherapy, chemotherapy should be administered in the centre where the radiotherapy department is located. When there is no Radiation Oncology department in the Reference Centre, patients must be sent to a Radiation Oncology Department having experience in treating head and neck cancer patients, e.g. typically treating more than 75 patients a year. In this setting, a formal partnership agreement needs to be reached between the Reference Centre and the Radiation Oncology Department. In the same setting, the Radiation oncologist in charge of H&N cancer patients must be physically present to participate to the multidisciplinary board meeting of the Reference Centre where the charts of the patients are discussed.

• Cytotoxic chemotherapy and biological therapies must be provided in a specific unit with nurses specialized in oncology and under the surveillance of physician specialized in medical oncology and with proven expertise in treating head and neck cancer patients. Because concomitant chemoradiation is currently a standard in the treatment of advanced head and neck cancer (as primary treatment and as adjuvant treatment postoperatively), the facilities for chemotherapy and radiotherapy administration must be on the same site. The medical oncologist(s) should have access to an outpatient ambulatory
centre to deliver chemotherapy but also to a regular dedicated oncology hospitalization unit, specialized in cancer patients management, to take care of the potential complications and to take care of the supportive treatment. One medical oncologist must be on call twenty-four hours a day and have access to an emergency room and intensive care unit.

- High quality speech and oral rehabilitation with “home” staff.
- Outpatient facility dedicated to head & neck cancer patients to allow short time and long term multidisciplinary surveillance after definitive treatment.

**Patient centred care**

- Typically, the patients referred to the Reference Centre should have a first outpatient visit within 2 weeks following call for appointment. The work up required to stage the tumour should be performed within the 3 next weeks following the first outpatient visit. After treatment decision discussed in the weekly multidisciplinary team meeting, the treatment should be initiated within the 3 weeks following this meeting. Typically, the delay between the first consultation in the Reference Centre and treatment starting should not exceed 6 weeks.
- Continuity of care (care covered 7 days a week by specialised staff)
- Support services for the patient (care coordinator: nurse coordinator in oncology – CSO/ Oncocoach dedicated to head & neck cancer patients, psycho-oncologist…)
- Collaboration to assure the continuity of care with a unit specialized in palliative care

**Minimal volume of patients**

The Reference Centre deals with all Head & neck Cancer. Today, only the centres treating a minimum of 100 new cases of head & neck cancer localized in the UAT (oral cavity, larynx, oropharynx, hypopharynx, nasopharynx, nose/middle ear and paranasal sinus), skull base, salivary gland, sarcomas of the head and neck and advanced head and neck skin cancer per annum should be accepted. This selection criterion should be based on the 2 or 3 years preceding the edition of this document. Clearly, centres with less than 50 new cases/year should no longer treat patients with head and neck cancer. As ideally, each Reference Centre in Head & Neck Cancer should treat a minimum of 200 new cases/year should no longer treat patients with head and neck cancer. As ideally, each Reference Centre should treat a minimum of 200 new cases/year but less than 200 patients/year must reach the required number after a transition period of 5 years. Because it is expected that all small centres will not be allowed to treat head & neck cancer patients, the optimal number of >200 new patients/year should be easily reached by the selected Reference Centres if the rules are strictly respected.

**Quality Assurance**

- An annual activity report is required, including transparency (number of new patients / type of cancer; diagnostic, treatment and outcome data; specific protocols for reporting and recording complications…).
- Continuous monitoring of risk and governance to ensure that clinical treatment is safe and effective.
- Development of clinical guidelines for diagnosis and care with regular updates.
- Compliance with existing guidelines and documentation of deviations from guidelines.
- Capacity to propose quality indicators (structure, process, outcomes).
- Short time and long term surveillance after definitive treatment.
• Obligatory registration of all head & neck cancers (incidence and follow-up data) to the National Cancer Registry – preferably the extended version such as already available for the subsite “oropharynx”.

**Research and other scientific activities**

• Current involvement in multicentre clinical protocols (RCTs, cohort studies, translational studies)
• Publications in peer-reviewed journals: at least 10 peer-reviewed publications during the last 10 years, by at least 3 members of the Reference Centre
• Publications of outcome data of the Reference Centre (see quality assurance)
• Link with a tumour bank

**Educational activities: Teaching and dissemination**

• Involvement in training and continuous education programs (annual or multi-annual training / educational programme for physicians, nurses, supportive disciplines)
• Organisation / communication in scientific congresses, by at least 3 members of the Reference Centre.