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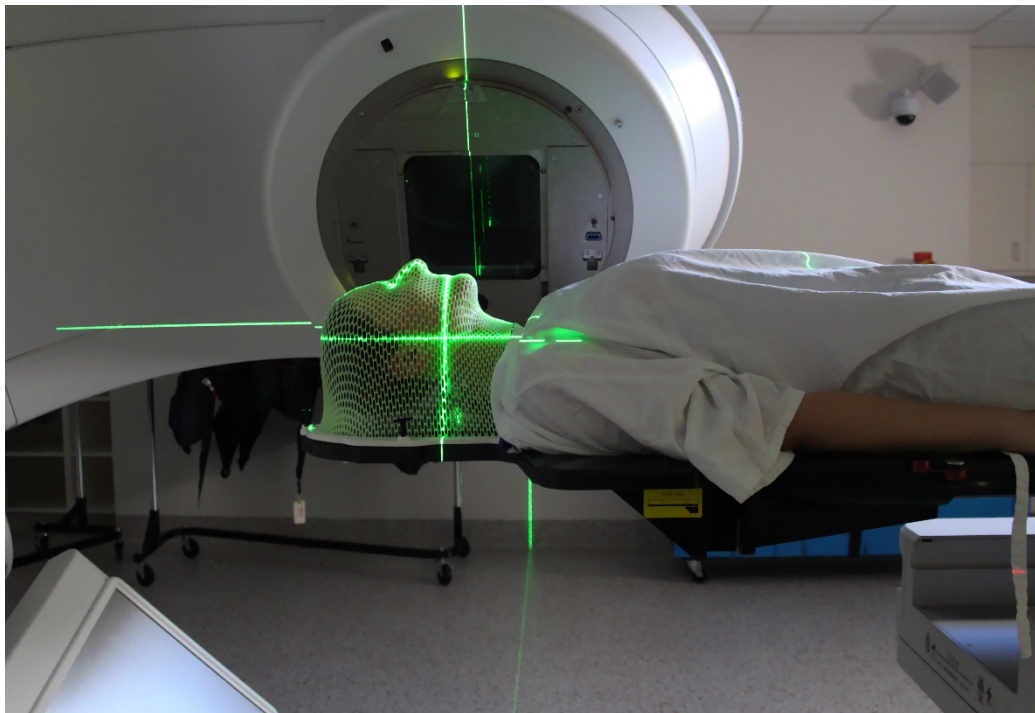Belgian Health Care Knowledge Centre

QUALITY INDICATORS FOR THE MANAGEMENT OF HEAD AND NECK SQUAMOUS CELL CARCINOMA

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- **Finally, this report has been approved by common assent by the Executive Board.**
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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
5FU	5-fluoro-uracil
95% CI	95% Confidence interval
AIC	Akaike Information Criterion
AIDS	Acquired immune deficiency syndrome
ATC	Anatomical Therapeutical Chemical
BCR	Belgian Cancer Registry
cI, cII, etc.	Clinical stage I, clinical stage II, etc.
CCI	Charlson Comorbidity Index
CIRS	Cumulative Illness Rating Scale
CRT	Chemoradiation
CSO	Coordinator of care in oncology ('Coordinateur de soins en oncologie')
CT	Computed tomography
DDD	Defined daily dose
DW-MRI	Diffusion-weighted magnetic resonance imaging
ECOG PS	Eastern Cooperative Oncology Group Performance Status
ENT	Ear, Nose and Throat
EORTC	European Organisation for Research and Treatment of Cancer
FDG-PET(/CT)	Positron-emission tomography (/Computed tomography) with the tracer molecule fluorodeoxyglucose
FOD – SPF	Federal Public Service ('Federale Overheidsdienst'/'Service Public Fédéral')
HIV	Human immunodeficiency virus
HNC	Head and neck cancer
HNOC	Head and Neck Oncology Centre
HNSCC	Head and neck squamous cell carcinoma
HPV	Human Papilloma Virus
HR	Hazard Ratio
ICD-9-CM	International Classification of Diseases, 9th Revision, Clinical Modification

ICED	Index of Coexistent Disease
ICU	Intensive Care Unit
IKNL	Netherlands Comprehensive Cancer Organisation ('Integraal Kankercentrum Nederland')
IMA – AIM	Intermutualistic Agency ('Intermutualistisch Agentschap'/'Agence Intermutualiste')
IMRT	Intensity-modulated radiotherapy
INSZ – NISS	Social security identification number ('Identificatienummer van de sociale zekerheid'/'Numéro d'identification de la sécurité sociale')
KCE	Belgian Health Care Knowledge Centre
KFI	Kaplan-Feinstein Index
KSZ – BCSS	Crossroads Bank for Social Security ('Kruispuntbank van de Sociale Zekerheid'/ 'Banque Carrefour de la Sécurité Sociale')
LND	Lymph Node Dissection
MDT	Multidisciplinary team meeting ('Multidisciplinair Oncologisch Consult' (MOC)/ 'Consultation Oncologique Multidisciplinaire' (COM))
MRI	Magnetic resonance imaging
MKG – RCM	Minimal Clinical Data ('Minimale Klinische Gegevens'/'Résumé Clinique Minimum')
MZG – RHM	Hospital discharge dataset ('Minimale Ziekenhuis Gegevens'/'Résumé Hospitalier Minimum')
NA	Not applicable
NHS	National Health Service (United Kingdom)
NICE	National Institute for Health and Care Excellence (United Kingdom)
NPV	Negative predictive value
OR	Odds Ratio
OS	Observed survival
pI, pII, etc.	Pathological stage I, II, etc.
PET(/CT)	Positron emission tomography (/Computed tomography)
PFS	Progression free survival
PORT	Postoperative radiation therapy

PPV	Positive predictive value
PS	Performance status
QI	Quality indicator
RIZIV – INAMI	National Institute for Health and Disability Insurance ('Rijksinstituut voor Ziekte- en Invaliditeitsverzekering'/'Institut National d'Assurance Maladie-Invalidité')
RT	Radiotherapy
RX	Radiography
SCC	Squamous cell carcinoma
SES	Socioeconomic status
SIGN	Scottish Intercollegiate Guidelines Network
TNM	Tumour – Node – Metastasis
UK	United Kingdom
US(A)	United States (of America)
UZ – CHU	University hospital ('Universitair ziekenhuis'/'Centre hospitalier universitair')
WHO	World Health Organization
WUHNCI	Washington University Head and Neck Comorbidity Index
X	Missing stage

■ SCIENTIFIC REPORT

1 INTRODUCTION

Since several years, the Belgian Health Care Knowledge Centre (KCE) and the Belgian Cancer Registry (BCR) have been engaged in quality improvement initiatives for cancer patients. To that end, they have defined an integrative quality system in oncology that starts with the development and implementation of clinical practice guidelines, followed by the development of a set of indicators aiming at measuring the quality of care and last but not least individual feedback provided to all hospitals, which can lead to corrective actions to improve quality.[1] At the national level, the steps of this improvement cycle have already been implemented for several cancers: rectum (in collaboration with PROCARE), breast, testis, oesophagus, stomach and lung.[2-6]

Building on these experiences, it was decided to set up a quality project for head and neck cancer for the following reasons: head and neck cancer presents an important burden and the management of head and neck cancer requires highly specialised care, but is very dispersed in Belgium.

1.1 Head and neck cancer in Belgium

Head and neck cancers (ICD10: C00-C14, C30-C32) are a **heterogeneous group of tumour entities**, which are anatomically close to each other, but differ in terms of aetiology, histology, and prognosis.[7] Typically, head and neck cancers develop in a population with large tobacco and alcohol consumption.[8] Other risk factors include viral infection (Epstein-Barr Virus for nasopharyngeal cancer and Human Papilloma Virus for oropharynx cancer), occupational exposure and radiation for major and minor salivary gland cancers.[9] About **91%** of all head and neck cancers are **squamous cell carcinomas**, 2% are sarcomas and the other 7% are adenocarcinomas, melanomas and not well specified tumours.[10]

Head & neck cancers occur preferentially in males. In 2016, there were 2 694 new diagnoses of head and neck cancer in Belgium, 2 005 in males and 689 in females.[11] In Belgium, head and neck cancer is the 4th most frequent tumour in males (6% of all malignancies) and the 11th most frequent in females (2%).[12] Compared to other European countries, Belgium has a very high incidence rate for head and neck cancer: for males, Belgium ranks second (after France) while for females, Belgium ranks fourth (after Denmark, France and the Netherlands).[12] In 2016, the mean age at diagnosis was 64 years.[11] By 2025, the annual number of patients diagnosed with head and neck cancer is expected to rise to more than 3 000.[12]

In Europe, age-standardised 5-year relative survival is the poorest for hypopharynx (25%), intermediate for oropharynx (39%) and oral cavity (45%) and the highest for larynx cancers (59%). With the exception of patients with laryngeal cancer, survival is significantly better in women than in men.[7] In Belgium, the **5-year relative survival rate** for the Belgian 2009-2013 cohort was about **51% in males and 58% in females**; a slight increase of the relative survival was observed over the 2004-2013 time span.[12]

1.2 Dispersion of care in Belgium

In 2014, the BCR published a report (with the financial support of the Vlaamse Liga tegen Kanker [a]) on the burden and clinical management of rare cancers - including head and neck cancers - in the Flemish Region for the period 2004-2007.[13] The report illustrates the **dispersion of care for patients diagnosed with head and neck cancers** (Table 1): for example the 384 patients with hypopharyngeal cancer had been treated in 29 different Flemish hospitals, with a median volume of 2 patients per centre (over the four year observation period) and a range between 1 and 56 patients per centre. Half of the patients (n=181) were treated in centres with a low-volume (defined as a hospital having taken care of less than forty patients diagnosed during the period 2004-2007).[13] Moreover, for some tumour sites (e.g. laryngeal and oropharyngeal cancer) **treatment schemes varied between low- and high-volume hospitals**: surgery seemed to be less frequently considered as the primary treatment in high-volume hospitals compared to low-volume hospitals. Yet, the authors admitted that this observation might have been confounded by the fact that radiotherapy had been considered with a rather high priority in the process of assigning patients to a centre.[13]

Table 1 – Summary of dispersion of head and neck cancer care in Flanders (2004-2007)

Tumour sites	N patients	N hospitals	Mean number of patients per hospital	Median number of patients per hospital	Range of number of patients per hospital
Hypopharynx	384	29	13.5	2	1 - 56
Larynx	1 227	55	22.0	11	1 - 170
Oral cavity	1 077	54	18.8	5.5	1 - 135
Oropharynx	811	46	17.0	5	1 - 115

Note: Not all cases presented in this table were squamous cell carcinoma.
Source: BCR, Rare Cancers in the Flemish Region - 2014[13]

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a   Vlaamse Liga tegen Kanker has been renamed Kom op tegen Kanker in 2014.

In the KCE report 'Organisation of care for adults with a rare or complex cancer' (2014) it was recommended that the diagnosis, treatment and follow-up of patients with head and neck cancers should be done in **reference centres**, in **collaboration with peripheral centres** with a program in oncology.[14] This approach was justified by the fact that head and neck cancers are **rare** [b] and given the **complexity** of diagnostic and staging procedures and the treatment and follow-up. Many patients require intensive multimodality treatments (including surgery, radiotherapy alone or combined with chemotherapy or targeted therapy) and prolonged rehabilitation/ long-term support to achieve adequate recovery. The disease as well as the treatments significantly impact on voice, swallowing, eating, drinking, smell, breathing, but also negatively affects appearance, social interaction and work capabilities.[15] Hence, the management of these patients also requires a **skilled and dedicated nursing and paramedical team** composed of clinical nurse specialist (Onco-coach/ Coordinator of care in oncology (CSO)), nutritionists, dieticians, speech therapists, dentists, psycho-oncologists, nursing staff with specific expertise in the management of head & neck cancer patients.[14] The concentration of care for patients with head and neck cancer has been successfully implemented in (among others) the Netherlands and Denmark.[16-18]

1.3 Measuring quality

As is sufficiently known, audit and feedback can reveal to what degree evidence-based recommendations are implemented, which outcomes are achieved in the population, which practices are associated with better outcomes and most importantly, what can be done to optimize the care in the future. Hospitals can benchmark their results against international and national results, identify best practices and that way improve their own practice.

According to Donabedian's classification, quality indicators can be categorized in **process indicators** (what is actually done in giving and receiving care), **outcome indicators** (states of health or events that follow care, and that may be affected by health care) and **structure indicators** (characteristics of providers and the health care system that affect the system's ability to meet the health care needs of individual patients or a community) (see Box 1).

The value-based health care framework of Porter et al. highly praises comprehensive outcome measurement to drive quality improvement. The complete set of all outcomes is what really matters to patients. Measured outcomes should reflect the quality of the whole care cycle, rather than outcomes of a single intervention, a single speciality or a single care episode. Measuring outcomes that are the result of a whole care cycle enforces all caregivers involved to accept joint accountability and work together towards quality improvement.[19]

However, data for comprehensive outcome measurement is often lacking, especially if retrospective databases are used. Data used to evaluate process indicators are more commonly available in administrative databases. Moreover, process indicators are more easily 'actionable', they show what precisely can be done differently to improve outcomes, under the condition that the effectiveness of the measured processes is supported by evidence.[19, 20]

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[b]   According to RARECARE layer 2, which is used for clinical decisions, all HNSCC are considered rare cancers.

Box 1 – Description of structure, process and outcome indicators

Structure indicators relate to the attributes of the settings in which care occurs. This includes material resources (such as facilities, equipment, and financing), human resources (such as the number and qualifications of personnel) and the organizational structure (such as medical staff, organization, methods of peer review, and methods of reimbursement).[20]

Process indicators refer to what is actually done in giving and receiving care, i.e. the practitioner's activities in making a diagnosis, recommending or implementing treatment, or other interaction with the patient.[20]

Outcome indicators attempt to describe the effects of care on the health status of patients and populations.[20]

2 OBJECTIVES, SCOPE & TERMINOLOGY

2.1 What this study aims at and does not aim at

The main objective of this study is to **develop a set of quality indicators** for the diagnosis and treatment of squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx and larynx and to **provide insight in the patterns of care and evaluate the outcomes of care** for these patients in Belgium. Auditing practice can reveal to what degree evidence-based recommendations are implemented, which outcomes are achieved in the Belgian population, which practices are associated with better outcomes and, most importantly, identify key areas for quality improvement where indicated.

Another objective of this report is to assess the volume-outcome relationship: do patients treated in high-volume hospitals have on average better outcomes than patients treated in low-volume hospitals?

Many indicators are analysed per hospital, which enables the analysis of the variability between hospitals. This approach also allows that individual feedback can be provided to the hospitals. Indeed, at the time of publication of this report, each Belgian hospital will receive an individual feedback report with its own results benchmarked to results obtained by other (blinded) hospitals. But it must be crystal clear: **this report does not intend to judge any individual caregiver or hospital**. The data used for this study do not always allow precise and correct comparison between individual hospitals as they are extracted from administrative databases originally not intended for quality measurements. Sample sizes are often small and residual confounding may exist, even after case-mix correction.

Deliberately, **all analyses were performed anonymously and are reported anonymously**. This approach is needed for an honest and constructive evaluation of the results, with a focus on quality improvement rather than competition between hospitals. Also less-than-perfect quality measurements can be informative and guide quality

improvement; yet using the same quality measurements as the basis for selective referral, pay-for-quality or public reporting of hospital rankings can be problematic.[19, 21] By avoiding a name-and-blame culture, we hope that all caregivers involved are encouraged to further improve the care for patients with head and neck cancer.

Last but not least, in the present report the processes of care and their outcomes are analysed for patients diagnosed in the period 2009-2014, thus before the publication of the KCE guidelines. The results should thus be regarded as a **baseline** for further follow-up of the quality of care in the future.

2.2 Preceding steps

Preceding this study, KCE published an evidence-based guideline for the diagnosis and treatment of squamous cell carcinoma of the oral cavity in 2014[22] and the oropharynx, hypopharynx and larynx in 2015.[22, 23] The quality indicators identified for the present study (cf. infra) were partly based on these guidelines.

2.3 Scope

The focus of the present study is limited to **squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx and larynx**; other head and neck cancer types (e.g. sarcoma of the head and neck) and head and neck cancers of other anatomical sites (e.g. nasal cavity, sinuses, nasopharynx, lip) were considered out of scope. Hence, from here on 'head and neck cancer' should be read as 'squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx and larynx'.

2.4 Target audience

The primary audience of this project are **caregivers and hospitals** that provide care for head and neck cancer patients. The results may also be of interest to other stakeholders, although their information needs may not fully be addressed. Patients for example may prefer other types of information, such as patient reported outcomes and experiences.

2.5 Terminology

In order to avoid Babel-like confusions, it is important to mention that throughout the whole report, the following definitions were used:

- **Systemic therapy**: chemotherapy and/or targeted therapy;

- **Concomitant chemotherapy** is defined as chemotherapy that started from seven days before the start of radiotherapy to any time during the RT series;

- **Induction chemotherapy** is defined as chemotherapy that started between 120 days and 7 days before the start of radiotherapy;

- **Any treatment**: surgery or RT with curative intent or chemotherapy or targeted therapy or palliative RT should have been performed. Start date of any of these treatments is then the first date of these treatments;

- **Non-palliative treatment**: surgery or RT with curative intent or chemotherapy or targeted therapy should have been performed. Start date of non-palliative treatment is then the first date of these treatments;

- **Curative treatment**: surgery with curative intent or RT with curative intent should have been performed, with or without systemic therapy. The start date of curative treatment is then the first date of surgery, RT or systemic therapy;

- **Palliative treatment**: the only palliative treatment that could be defined in this project was palliative radiotherapy (see section 3.3.2.1).

3 METHODOLOGY

This chapter presents an overview of the methodology followed to identify, select, measure and interpret quality indicators related to the diagnosis and treatment of head and neck cancer. It must be emphasized that every single step in this process was thoroughly discussed with the clinical experts (see colophon) during no less than 21 meetings and through a very intensive e-mail communication.

The clinical experts, from various horizons with regards to specialty and with profound experience in the diagnosis and treatment of patients with head and neck cancers, work in academic and non-academic centres, geographically spread over the country and know the Belgian context (e.g. fees, reimbursement rules) very well. They were selected from the group of experts that participated in the development of the two KCE guidelines that preceded this report (see section 2.2).[22, 23]

3.1 Step 1: Identification of the target population: data selection and linkage of databases

3.1.1 Selection of the study population in the Belgian Cancer Registry database

A total of 15 339 head and neck cancer patients (ICD-10: C01-C14 and C30-C32) diagnosed in 2009-2014 were identified in the Belgian Cancer Registry (BCR) database. This concerns all patients (with Belgian nationality or foreigners) with official residence in Belgium at the time of diagnosis. From this population, only patients with an oral cavity, oropharynx, hypopharynx or larynx squamous cell carcinoma (SCC), according to the criteria of RARECAREnet – layer 2, were selected for the study (see Appendix 1).

Furthermore, a number of exclusion criteria were applied (see Figure 1):

1. Patients for whom no link could be made with the database of the Intermutualistic Agency ('Intermutualistisch Agentschap' – 'Agence Intermutualiste', IMA – AIM, see section 1.1.1), because quality indicators cannot be calculated without these data;

2. Patients whose incidence date is the same as the date of death: quality of care can obviously not be evaluated for those patients;

3. Patients whose incidence date is the date of lost to follow-up: these are patients who lived in Belgium at time of diagnosis, but moved abroad when first checked for their vital status at the Crossroads Bank for Social Security ('Kruispuntbank van de Sociale Zekerheid' - 'Banque Carrefour de la Sécurité Sociale', KSZ – BCSS, see section 3.1.4);

4. Patients with multiple invasive tumours registered in the BCR database. This exclusion criterion ensures that the population included in the analysis consists only of patients with one single SCC of the head and neck and it increases the probability that the identified medical procedures were indeed performed for that SCC of the head and neck.

The **incidence date** is the date of first histopathological confirmation of the tumour. When there is no histopathological confirmation, the incidence date is the day of the technical procedure or clinical investigation leading to the diagnosis of cancer.

A total of 6 094 patients were excluded from the study (39.7%). The resulting **study population consists of 9 245 patients (60.3%) diagnosed in 2009-2014 with a head and neck SCC**. The characteristics of the study sample are described in section 4. For further analyses, this study population is divided into four anatomic sites:

1. 2 665 patients with a SCC of the oral cavity

2. 2 745 patients with a SCC of the oropharynx

3. 1 137 patients with a SCC of the hypopharynx

4. 2 698 patients with a SCC of the larynx

Figure 1 – Selection of the study population (N=9 245)
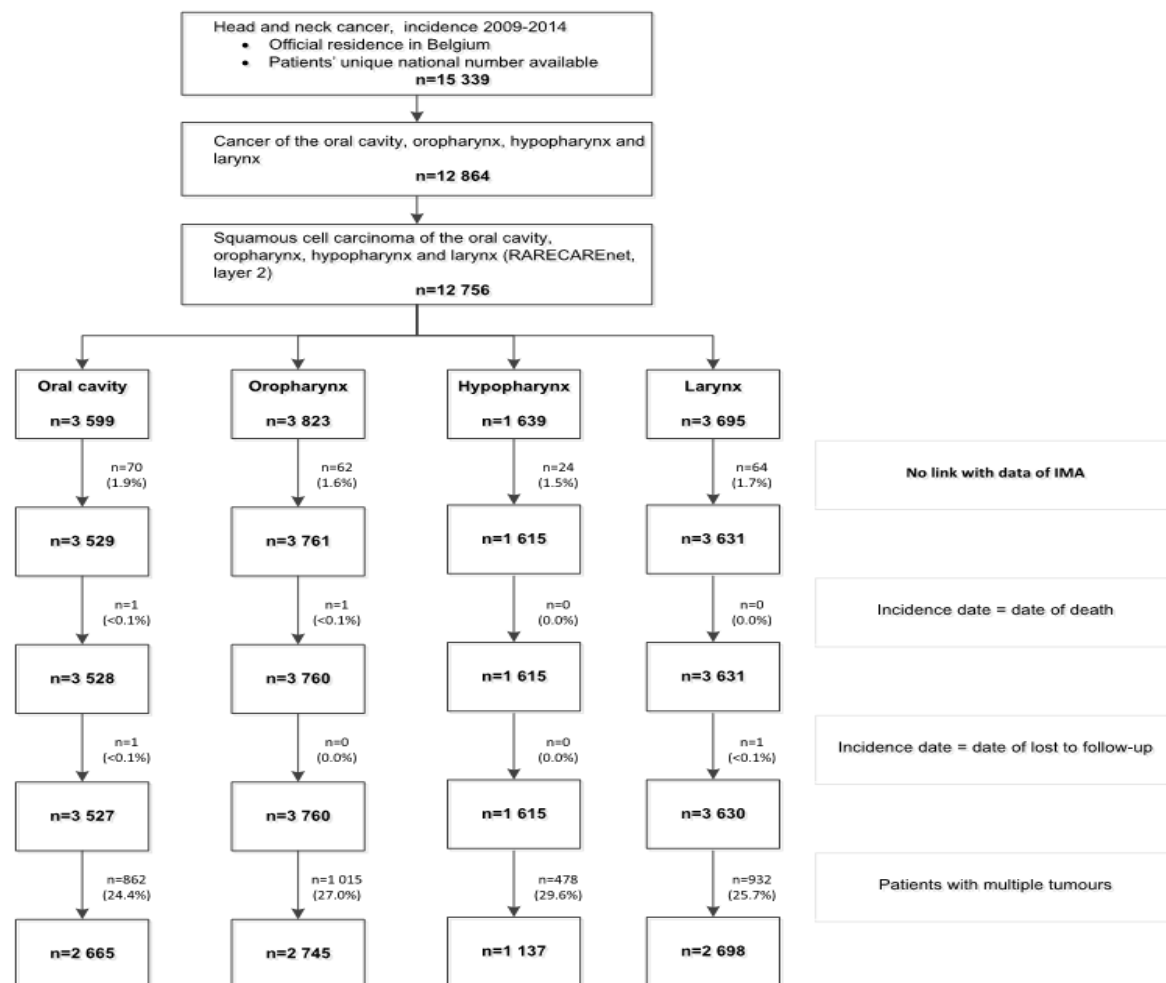
Source: BCR – IMA

3.1.2 Linkage with health insurance data

In Belgium, physicians are mainly paid fee-for-service. Compulsory health insurance pays for medical services on the basis of a fee schedule, called 'nomenclature' (see Box 2). Since 2009, the Belgian Cancer Registry is authorized to link data from its database with data on cancer-related diagnostic and therapeutic procedures and pharmaceuticals.[24] These data are obtained from all seven Belgian sickness funds via the Intermutualistic Agency (IMA – AIM). Via this linkage procedure, the Belgian Cancer Registry receives for each registered patient, health insurance data starting from 1 January of the year preceding the incidence year, until 31 December of the fifth year after the incidence year. These data are further mentioned as IMA – AIM data. At the start of this study, IMA – AIM data up to June 2016 were available at the Cancer Registry.

From the originally selected 12 756 patients, 12 536 (98.3%) could be linked to the IMA – AIM database. Patients for whom no information was available in the IMA – AIM database were probably not affiliated to one of the seven Belgian sickness funds or had an invalid Social Security Identification Number (INSZ – NISS).

Box 2 – The RIZIV – INAMI nomenclature

Medical and paramedical services covered by compulsory health insurance are listed in a fee schedule, called 'nomenclature', which lists almost 9 000 unique covered services. The list of reimbursable codes contains for each item the professional qualification needed to be eligible for reimbursement, a code-number, a description of the item, a key letter according to the medical specialty, a coefficient and application rules. The coefficient gives for each procedure the relative value compared to other procedures with the same key letter. Multiplying the coefficient by the value of the key letter determines the amount of payment to the provider concerned (i.e. the fee).

The type of reimbursable benefits and their amounts (total fee and reimbursement) are determined through a process of negotiations with the various parties involved within RIZIV – INAMI, all within pre-set budgetary limits. The National Commission of Sickness Funds and Providers, the so-called 'Medico-Mut' negotiates on the tariffs, and more specifically, on the value of the key letter. The negotiated fee or 'convention tariff' is settled in agreements (for physicians and dentists) and conventions (for other healthcare providers).

A disadvantage of working with IMA – AIM data is that they have no direct link with the indication for the intervention and that the nomenclature description is often unspecific. In order to meet to the former drawback as much as possible, only interventions performed near the incidence date were selected so that procedures that were done for other indications could be excluded as best one can. In the databases, small deviations in the incidence date and the date of the medical act are possible. Therefore, time frames were used to link the IMA – AIM data to the cancer diagnosis. Unless otherwise specified, the following time frames were used in this study:

- For diagnostic procedures and multidisciplinary team meeting (MDT, 'Multidisciplinair Oncologisch Consult (MOC)' – 'Consultation Oncologique Multidisciplinaire (COM)'), a symmetric time frame of three months before until three months after the incidence date was used;

- For therapeutic procedures, an asymmetric time frame starting one month before the incidence date until six months after the incidence date was used;

- Pre-operative treatment (radiotherapy or systemic therapy) was defined as treatment starting one month before the incidence date until the date of surgery with curative intent (date of surgery excluded);

- Adjuvant treatment was defined as treatment starting on the date of surgery with curative intent until six months after surgery.

One month was defined as thirty days.

3.1.3   Linkage with hospital discharge data

For each patient seen in a Belgian hospital (inpatient and day care), hospitals have to send administrative and medical data (more precisely, Minimal Hospital Data ('Minimale Ziekenhuis Gegevens'/'Résumé Hospitalier Minimum', MZG – RHM[c]), defined in a Royal Decree to the Federal Ministry of Health (FOD – SPF).[25] These data contain (among others) the diagnosis for hospitalisation, the principal and secondary diagnoses and the procedures performed during the hospital stay. Over 98% of the inpatient hospital stays charged to the health insurance are linked to MZG – RHM.[26] The medical data in MZG – RHM are based on the International Classification of Diseases-9th Revision-Clinical Modification (ICD-9-CM), which is a system of assigning codes to diagnoses and procedures associated with hospital utilization.[27]

Since March 2016, the Belgian Cancer Registry is authorized to receive hospital discharge data linked to a predefined set of BCR data (on a coded level) for patients in the cancer registration database with incidence date from 2004 onwards.[28] For each registered patient, the BCR is allowed to receive data from 1 January of the year preceding the incidence year, until 31 December of the year following the incidence year. Currently, hospital discharge data from 2004 until 2014 are available at the BCR.

For this study, hospital discharge data within the year preceding the start of the cancer treatment (or the year preceding the incidence date if no treatment was recorded) were used to estimate the presence of comorbidities in patients with SCC of the head and neck (see section 3.3.5). From the 9 245 patients included in the study, hospital discharge data were available within the defined time frame for 8 812 (95.3%) patients. Patients for whom no data were available, were probably not admitted in hospital (neither for day care nor for inpatient care) during the selected time period,

although some underreporting in the MZG – RHM (e.g. due to technical or administrative problems) cannot be ruled out.

3.1.4   Vital status

Information with regard to the vital status of the included patients was retrieved from the Crossroad Bank of Social Security ('Kruispuntbank van de Sociale Zekerheid' - 'Banque Carrefour de la Sécurité Sociale', KSZ – BCSS) based on the patients' unique social security identification number (INSZ – NISS). Using this active follow-up method, patients were followed up until 14 December 2017.

3.2   Step 2: Identification and selection of possible quality indicators

3.2.1   Identification of possible quality indicators

Possible quality indicators were identified from peer-reviewed papers (indexed literature; see Appendix 2.1 for the search strategy Ovid Medline), reports published by international healthcare agencies (grey literature; http://www.qualitymeasures.ahrq.gov, http://www.nice.org.uk, http://www.iknl.nl, http://www.healthcareimprovementscotland.org, and http://www.clinicalaudit.nl) and the KCE guidelines on oral cavity cancer,[22] and on oropharyngeal, hypopharyngeal and laryngeal cancer.[23] and the guidelines on the management of head and neck cancer published by the German Cancer Society (DKG),[29] Netherlands Comprehensive Cancer Organisation (IKNL)[30] and Scottish Intercollegiate Guidelines Network (SIGN)[31] were also screened. In addition, Google was searched using the key words 'head and neck cancer' and 'quality indicator'. The main searches were conducted in November 2015.

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[c]   MZG – RHM: Hospital discharge dataset ('Minimale Ziekenhuis Gegevens'/'Résumé Hospitalier Minimum'). In 2008, the initial minimal clinical data (MKG – RCM) gathered by the hospitals were replaced by minimal

hospital data (MZG – RHM) offering more information and a higher and more reliable linkage potential. Because of the suboptimal linking with MKG – RCM data (available until 2007), it was decided not to use the MKG - RCM data and start from incidence year 2009 onwards.

3.2.2   Selection process and results

The Medline search yielded 84 unique citations (after exclusion of four duplicates and twenty references in a language other than English, French or Dutch). Based on title and abstract two papers were included for full-text evaluation. This evaluation resulted in the inclusion of one paper that reported quality indicators.[32] From the grey literature five additional papers and reports were selected as sources for quality indicators.[15, 32-36] An overview of the selected documents is given in Appendix 1.2, Table 12. In a final step, the clinical experts were asked to amend the list with missing indicators, which resulted in twelve additional indicators.

The initial long list of quality indicators identified in the above mentioned sources contained 176 indicators, including those suggested by the clinical experts.

Indicators that referred to the same concept were merged in a single indicator whenever possible. Furthermore, indicators were rephrased for clarity and consistency. Finally, indicators that were not in agreement with Belgian clinical recommendations were adjusted or removed. This step resulted in a list of 107 indicators of possible interest. The 69 indicators that were excluded in this step can be found in the Supplement (Appendix 2.3, Table 13).

The list of 107 indicators was used as the starting point for the assessment of indicators by a panel of eleven clinical experts (see colophon). First the members of the panel were asked to score each quality indicator on its relevance. To be relevant, an indicator needed to reflect an important health issue or an aspect of the health system functioning that matters to the health of the population group in question and assist in monitoring health system performance and be meaningful to stakeholders.

To that end a five-point scale was used:

     5 = Top priority: should be included

     4 = Moderate priority: can be included

     3 = Some priority: inclusion unsure

     2 = Little priority: likely not to be included

     1 = No priority: should not be included

Each clinical expert received one vote; the Belgian Cancer Registry and KCE each received one vote, leading to thirteen votes in total. Indicators were then ranked according to the received scores. (For your information, scores received on relevance are summarized in Appendix 2.4, Table 14).

The decision on inclusion or exclusion of indicators was taken by consensus during two meetings (held on 11 January 2016 and 12 February 2016) with the clinical expert panel, KCE and BCR. During these consensus meetings criteria other than relevance (e.g. measurability, actionability) were also taken into account. The discussion mainly focused on the 58 indicators identified as being highly relevant (i.e. ≥ 70% of assessors scoring 4 or 5). It was agreed to exclude the 49 indicators with a lower relevance (see Appendix 2.4, Table 15). Of the 58 indicators originally identified as having a high relevance, 12 were excluded (the rationale for exclusion is mentioned in Appendix 2.4, Table 16) and 14 were merged with another indicator (Appendix 2.4, Table 17), leaving 32 indicators.

During the second consensus meeting, a 33rd indicator was added because of its high perceived relevance ('Proportion of patients with metastatic or recurrent head and neck squamous cell carcinoma (HNSCC) being included in a clinical trial').

3.2.3 Measurability of selected quality indicators

The 33 quality indicators were judged for their measurability with available data by experts from KCE and BCR. To that end, the availability of administrative data for every single element of the quality indicator was evaluated. Fifteen quality indicators were considered measurable and eighteen not (Appendix 2.4, Table 18).

At this stage it was also decided by consensus to combine the relative and observed survival after a diagnosis of HNSCC into one single indicator, leaving fourteen indicators. Since the inclusion in the study was based on the histological confirmation of a squamous cell carcinoma, the quality indicator 'Proportion of patients with HNSCC who have a cytological or histological diagnosis before treatment' was considered redundant and hence excluded (Appendix 2.4, Table 19).

One of the 13 indicators (staging with MRI and/or CT) was judged to be only partially measurable (in the absence of specific nomenclature codes for MRI), but nevertheless fully elaborated as there was sufficient information available to allow a meaningful interpretation.

3.2.4 Final selection of quality indicators to be fully elaborated

Thirteen indicators were fully elaborated, and form the basis of the report; they are presented in Table 2. According to Donabedian's classification, quality indicators were categorized in process, structure and outcome indicators (Table 2, last column).[37] The majority of the selected indicators were process indicators, whereas only two indicators assessed outcome and one indicator was selected to measure the structure. The following quality dimensions were covered: effectiveness, appropriateness, continuity, safety and timeliness. No indicator addressed patient-centeredness, efficiency or equity.

In the elaboration of the 13th QI, i.e. hospital volume of patients with HNSCC treated, emphasis was laid on the association between volume and outcomes (i.e. survival and 30-day mortality, see section 5.5).

Table 2 – Final selection of thirteen quality indicators

Category	Quality Indicator	S/O/P
Generic indicator	The 1, 2 and 5-year observed and relative survival after a diagnosis of HNSCC	O
Diagnosis and staging	Median time between incidence date and start of first treatment with curative intent	P
	Proportion of non-metastatic HNSCC patients who underwent MRI and/or contrast-enhanced CT of the primary site and draining lymph nodes before treatment with curative intent	P
	A. Proportion of patients with HNSCC who have their cTNM stage reported to the Belgian Cancer Registry (BCR) B. Proportion of patients with HNSCC who had surgery, who have their pTNM stage reported to the BCR	P
	Proportion of patients with HNSCC who underwent FDG-PET(/CT) before start of treatment	P
Treatment	Proportion of patients with early stage (cI or cII) HNSCC who were treated with a single-modality approach	P
	Proportion of patients with non-metastatic T4a laryngeal cancer who underwent total laryngectomy	P
	Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was completed within thirteen weeks after surgery	P
	Proportion of medically fit patients with locally-advanced (stage III and IV) non-metastatic HNSCC treated with primary RT, who received concomitant platinum-based chemotherapy	P
Management of lymph nodes	Proportion of patients with node-positive HNSCC treated with primary (chemo)radiotherapy, in whom a diagnostic evaluation of the neck with PET(/CT) or (DW-) MRI was performed not earlier than three months after completion of the primary therapy	P
	Proportion of surgically treated patients with HNSCC and cN0M0/x with any T stage (except T1 glottic cancer), who underwent elective neck dissection	P
Safety of care	Proportion of patients with HNSCC who die within 30 days of treatment with curative intent	O
Treatment volume	Volume of patients with HNSCC treated (Association between volume of patients with HNSCC and outcome)	S

S: structure; O: outcome; P: process

3.3 Step 3: Operationalization of indicators

3.3.1 Technical fiches

For each selected quality indicator, a technical fiche was constructed detailing the rationale behind the indicator and its definition (type of indicator, description, numerator and denominator). Each indicator was translated in an algorithm including all in- and exclusion criteria. For each variable, relevant nomenclature codes were searched (see section 3.3.2 and Appendix 3.1-Appendix 3.3). Whenever applicable, a target was defined by expert consensus before the analysis of the QI. Furthermore, the need for subgroup analyses, risk adjustment and sensitivity analyses was evaluated. The technical fiches of all quality indicators are included in Appendix 7.

3.3.2 Defining diagnostic and therapeutic procedures based on health insurance data

3.3.2.1 Selection of nomenclature and ATC codes

For each diagnostic and therapeutic procedure that is used in one of the quality indicators, nomenclature codes were selected in the IMA – AIM database and then discussed with the research team and the clinical experts.

Diagnostic procedures

For diagnostic tests, the same nomenclature codes were used for the four anatomic sites under study. For example, the same nomenclature codes were used to invoice a PET-scan. This was not the case for biopsy and MRI. For example, for oral cavity and oropharynx the nomenclature codes for an MRI of the head and for an MRI of the neck were included, while for hypopharynx and larynx only the nomenclature codes for a MRI of the neck were included.

Surgical procedures

For surgery with curative intent, the selection was made for each anatomic site (i.e. oral cavity, oropharynx, hypopharynx, and larynx) separately. The selection of nomenclature codes that corresponded with the surgical interventions that were performed in the frame of SSC of the head and neck turned out to be very difficult. More precisely, several nomenclature codes describe interventions that can be performed for diagnostic purposes, but may also be performed with curative intent for small tumours. Therefore, a distinction was made between small and large tumours on the one hand, and minor and major surgical procedures (see Appendix 1.1, Table 38 – Table 47) on the other hand. Small and large tumours were distinguished based on the tumour size (T) as defined by the TNM-classification: T1 and T2 were considered small tumours while T3 and T4 were considered large tumours. The clinical T was prioritized and if the clinical T was missing, the pathological T was used. In case both clinical and pathological T data were missing (Tx), the tumour was considered a small tumour. The use of TNM-rules depended on the incidence year of the tumour: for the incidence year 2009 the sixth edition of the TNM was used,[38] while for incidence years 2010-2014 the seventh edition of the TNM was used.[39]

For large tumours (T3,4) only major surgical interventions were considered to have a curative intent, while for small tumours (T1,2,x) both minor and major surgical interventions were considered to have a curative intent.

To get more insight in the billing practices for surgical procedures, a check was performed with six hospitals during a pre-validation phase. During this phase, data from patients for whom it turned out to be difficult to determine whether or not they had surgery with curative intent were transferred to the hospital to get more insight. This phase resulted in a further fine tuning of the selection of nomenclature codes. Preliminary results were then again discussed with the clinical experts to further optimise the nomenclature selections. In a final step, these nomenclature selections were tested in a validation phase with sixteen hospitals (see section 3.5.3). For all hospitals together, the results of this validation phase for surgical procedures were within the predefined limits of 5% discordance between hospital data and health insurance data. However, on an individual hospital and patient level, inconsistencies remained (see section 3.5.3).

Because of the importance of surgery with curative intent for the calculation of many quality indicators, it was checked whether a better concordance could be achieved with hospital discharge data (MZG – RHM). Relevant ICD-9-CM codes for MZG – RHM procedures registered within the time frame one month before until six months after the incidence date were selected (see Appendix 3.4). This selection was based on an international publication (McDevitt et al., 2016[40]) and on the advice of the clinical experts. Validation of the MZG – RHM results was complicated by the fact that MZG – RHM data are not available to the non-coded patient-level used for the validation phase. Therefore, a comparison with the 'gold standard' data provided by the hospitals during the validation phase was not possible. However, when comparing MZG – RHM data with IMA – AIM data in a separate database of patients with SCC of the head and neck available for the BCR, identifying surgery with curative intent via MZG – RHM data offered no added value when compared to surgery identified based on IMA – AIM data. The proportion of patients undergoing surgery with curative intent based on MZG – RHM data was too low according to expert opinion. Therefore, it was decided that the identification of surgical procedures would only be done based on IMA – AIM data (and not on MZG – RHM data).

Lastly, at the time of the validation phase, it was decided that it was too hard to distinguish surgery with curative intent from diagnostic procedures for small hypopharynx and larynx tumours (T1,2,x) and therefore they were not included in the validation phase (see section 3.5.3). However, clinical experts argued that excluding this large group of patients from the analyses of the quality indicators was not an option. Therefore, upon experts' advice, two changes in the definition of surgery with curative intent were made: (a) if a minor surgical procedure was followed by radiotherapy within sixty days, the minor surgical procedure was considered as a diagnostic procedure, (b) when two major surgical procedures took place within sixty days, the surgery with the highest key value (see Box 2) was selected as the surgical procedure with curative intent.

After these changes were applied, the nomenclature codes (identified in the IMA – AIM data) for small hypopharynx and larynx tumours were compared with the pathology reports for a sample of patients. Both patients who had received surgery with curative intent according to our nomenclature selection, as well as patients for whom no surgical codes had been identified in the nomenclature code selection, were included in the sample. The objective was to check whether the surgical codes (for surgery with curative intent) were correctly selected from the IMA – AIM data. The results showed that the selection of nomenclature codes for surgery with curative intent was adequate. However, these checks showed that including lymphadenectomy in the algorithm to define surgery with curative intent (see section 3.3.2.2) induced errors for hypopharynx. After adapting the algorithm for surgery with curative intent of small hypopharynx SCC, the concordance between IMA – AIM data and the pathology reports was 96% for T1,2,x small laryngeal SCC, and 88% for T1,2,x small hypopharyngeal SCC. Although this result for small hypopharyngeal SCC was lower than the predefined 95%, it was agreed to accept this larger deviation since the exclusion of small hypopharyngeal SCC was not an option for the clinical experts and the number of small hypopharyngeal SCC was low. Moreover, no alternative approach to define surgery with curative intent was left. Yet, this lower concordance calls for a careful interpretation of the results obtained for small hypopharyngeal SCC.

More information concerning the definitive algorithm used to define surgery with curative intent in this study can be found in section 3.3.2.2.

Radiotherapy

For all analyses short series of radiotherapy (category 1, maximum 10 fractions) were considered as palliative radiotherapy, while longer radiotherapy series were considered to be performed with curative intent (categories 2 to 8, between 11 and 35 fractions, see Appendix 3.3.1).

When interpreting the results, some limitations should be taken into account:

- The start date of radiotherapy is not always available in the IMA – AIM database. According to the billing rules, hospitals should record each fraction separately and invoice the total RT scheme on the last day of the RT schedule.[41] A check of the database revealed that 81.3% of all RT schemes were recorded according to the billing rules; in five RT centres almost none of the RT schemes were invoiced according to the rules. Regularly, only the last session date is registered in the IMA – AIM database. For these cases the BCR constructed an algorithm to estimate the start date of radiotherapy based on the simulation date. If also the simulation date was not available, the start date was estimated based on the end date and the duration of the series of similar patients for whom the start date was available in the IMA – AIM database.

- Another limitation is that the fee for the whole scheme is always billed, regardless of the number of fractions that was actually given. Therefore, it is not possible to distinguish patients who completed the whole RT scheme from patients who received RT fractions but who stopped their treatment before it was completed.

Systemic therapy

The list of systemic therapy products (i.e. chemotherapy and targeted therapy) given as treatment for SCC of the head and neck, was selected based on discussions with the clinical experts; they were then identified in the IMA – AIM database using the Anatomical Therapeutical Chemical (ATC) codes issued by the WHO (see Appendix 1.1, Table 54 and Table 55).

One difficulty in defining systemic therapy based on IMA – AIM data, is that it is not possible to discern different series of systematic therapy.

Palliative treatment

The only palliative treatment that could be defined in this project was palliative radiotherapy (i.e. radiotherapy category 1, maximum 10 fractions). Although systemic therapy only is not regarded as a curative treatment option for head and neck SCC, it was opted to report the results of patients who had received only systemic therapy separately.

The nomenclature and ATC selections can be found in Appendix 3.3.2 (Table 49).

3.3.2.2 Algorithm used to define surgery with curative intent

As previously described, the selection of nomenclature codes that correspond with 'surgery with curative intent' for head and neck SCC was not straightforward. An additional problem arose from the nomenclature attesting rules which stipulate that the combination of certain procedures on the same day is (for budgetary reasons) not allowed. More precisely, when for instance lymphadenectomy or reconstructive surgery is performed on the same day as surgery of the primary tumour, it is not allowed to attest both procedures when the same incision is used. Hence only one of them is recorded in the IMA – AIM database. Therefore, after thorough discussion with the clinical experts, an algorithm to identify surgery with curative intent from the administrative databases was constructed, taking into account minor and major surgical procedures, lymphadenectomy, and reconstructive surgery.

Algorithm for small tumours (T1, 2, x):

1. If only one minor or one major surgical procedure was performed within six months after diagnosis: this surgical procedure was selected as the surgery with curative intent; an exception was made for hypopharynx and larynx: if the minor surgical procedure was followed by radiotherapy within sixty days, the minor surgical procedure was considered a diagnostic procedure (biopsy);

2. If two major surgical procedures (both within six months after diagnosis) took place within sixty days: the surgical procedure with the highest key value (see Box 2) was selected;

3. If two major surgical procedures (both within six months after diagnosis) took place more than sixty days after each other, the first surgical procedure was selected;

4. If both a major and a minor surgical procedure (both within six months after diagnosis) took place and the major surgical procedure occurred before or maximum sixty days after the minor surgical procedure, the major surgical procedure was selected as the surgical procedure with curative intent;

5. If both a major and a minor surgical procedure (both within six months after diagnosis) took place and the minor surgical procedure occurred more than sixty days before the major surgical procedure, the minor surgical procedure was selected as the surgical procedure with curative intent. In this case, the major surgical procedure was considered as a re-intervention;

6. If no major or minor surgical procedure was selected, and a lymphadenectomy (within six months after diagnosis) took place without radiotherapy with curative intent (within six months after diagnosis), the lymphadenectomy was selected as surgical procedure with curative intent for the primary tumour; (as was explained above, rule 6 was not applied for small hypopharyngeal SCC because an additional check comparing the IMA – AIM data and the pathology protocols, revealed that the inclusion of this rule led to errors);

7. If the previous rules did not apply, a reconstructive surgical procedure was taken into account when performed within six months after diagnosis.

A similar algorithm was built for large tumours (T3, 4). The main difference between the algorithm for large tumours and the algorithm for small tumours is the inclusion of minor surgical procedures. Minor surgical procedures were not considered as surgery with curative intent for large tumours and were therefore not included in this algorithm.

1. If only one major surgical procedure was performed within six months after diagnosis: this surgical procedure was selected as the surgical procedure with curative intent;

2. If two major surgical procedures (both within six months after diagnosis) took place within sixty days: the surgical procedure with the highest key value (see Box 2) was selected;

3. If two major surgical procedures (both within six months after diagnosis) took place more than sixty days after each other, the first procedure was selected;

4. If no major surgical procedure was selected, and a lymphadenectomy (within six months after diagnosis) took place without radiotherapy with curative intent (within six months after diagnosis), the lymphadenectomy was selected as the surgical procedure with curative intent for the primary tumour; rule 4 was not applied for large hypopharyngeal SCC because an additional check comparing the IMA – AIM data and the pathology protocols revealed that the inclusion of this rule led to errors;

5. If the previous rules did not apply, reconstructive surgery was taken into account if performed within six months after diagnosis.

Note: In the nomenclature, there is no specific code to invoice a salvage neck dissection. This procedure is invoiced with the same nomenclature code as another neck dissection. Neck dissection was not taken into account in the surgery algorithm if the patient was primarily treated with radiotherapy.

3.3.3   Defining the treatment scheme of the patient

For each patient, a treatment scheme was defined based on the IMA – AIM data. First we started with defining surgery with curative intent for the patients, based on the above described algorithm. If surgery with curative intent was found for a patient, pre-operative and adjuvant treatments were defined. When no surgery with curative intent could be identified, radiotherapy and systemic therapy were defined. Based on these treatment modalities, treatment schemes were defined and grouped into six categories:

* surgery with curative intent

* (systemic therapy/) radiotherapy with curative intent

* (systemic therapy/) radiotherapy with curative intent followed by surgery

* systemic therapy only

* palliative treatment

* no treatment (identified in the database)

To define the centre of main treatment (see section 3.4), these six treatment schemes were further grouped into four main treatment categories: the treatment scheme '(systemic therapy/) radiotherapy with curative intent' was taken together with the treatment scheme '(systemic therapy/) radiotherapy with curative intent followed by surgery' and the treatment schemes 'palliative treatment' and 'no treatment (identified in the database)' were taken together as 'no treatment'. The treatment schemes 'surgery with curative intent' and 'systemic therapy only' remained as such.

3.3.4   Statistical analyses

3.3.4.1   Visualisation of centre variability

Funnel plots

For most quality indicators, the observed indicator result per hospital is visualised in funnel plots. A funnel plot is a scatter plot of the estimate of an indicator on the vertical axis versus its precision on the horizontal axis. This precision equals the inverse of the standard error of the estimate (1/SE) or the square of it (1/SE^2).

Moreover, when a reference or population value can be assigned and a distribution assumed, prediction limits can be added to the funnel plot. These control limits are the upper and lower values of the expected (100-α)% prediction interval by centre size given the reference value and the distribution (α often equals to 5 or 1). It is further assumed that all units have the same underlying population value. These prediction limits allow the comparison of the variability of the observed estimates with the expected variability. The funnel plots for the indicators presented in the report take the observed overall indicator result as the population or reference value.

The precision on the proportion of a binary indicator is proportional to the unit size. The funnel plot for a binary proportion therefore obtains an elegant representation: the estimates are plotted versus the number of observations of the hospitals. The binomial distribution is used for the construction of the 95% and 99% funnel limits for the binary indicators.

The funnel plots for the observed and relative survival results are plotted versus the precision, which does not exist for an observed survival of 0 or 100%. Hospitals with an observed survival of 0 or 100% were therefore not displayed on the funnel plots. The prediction limits on the survival funnel plots were constructed assuming an asymptotic normal distribution using a log-log transformation.

As the underreporting of TNM stage information (see section 5.1.3) may bias the results, those centres which reported for less than 50% of their assigned patients stage information to the BCR, were represented differently (i.e. by an open triangle) in the funnel plots.

Forest plots

The centre comparison in the funnel plots does not take into account differences in indicator results between hospitals due to differences in patient case mix (see section 3.3.5). Therefore, Odds Ratios (OR) or Hazard Ratios (HR) adjusted for case mix are visualised in forest plots.

A forest plot is a scatter plot showing an estimate (e.g. an outcome variable, a regression parameter) with its confidence interval on the vertical axis versus unit ranking on the horizontal axis. The OR and HR estimates are relative to the 'average hospital'. A horizontal reference line is added to the forest plots which represents the 'average patient', obtained by a weighted average of the hospital OR/HR with the number of patients per hospital divided by the total number of patients as weight.

If the reference line cuts the confidence interval, the estimate for that hospital is not statistically significantly different from the reference (at the confidence level applied, mostly 95%). If the confidence interval does not contain the reference value, the estimate for that centre is statistically significantly different from the reference (at the significance level applied).

3.3.4.2 Post-operative and post-RT mortality

ESTIMATION OF POST-TREATMENT MORTALITY

Post-treatment mortality was calculated at three time points: 30, 60 and 90 days. The mortality was calculated as the ratio of the patients died within the specific time period and the number of patients alive at time zero. Patients censored within the specific time interval were not considered in the denominator. The day of surgery or the date of last RT fraction were used as time zero for post-operative and post-RT mortality, respectively.

MODELLING OF POST-TREATMENT MORTALITY

General modelling strategy

The post-treatment mortality at 30 days was modelled with logistic regression, using death within 30 days as the event. Baseline patient case-mix variables taken into account were: gender, age group at diagnosis, WHO performance status, combined stage, anatomic site, Charlson

Comorbidity Index (CCI) adapted (cf. 3.3.5) and number of previous inpatient bed days. All case-mix variables were considered as covariates in the logistic model. Second order interactions between the main terms were evaluated in a backwards elimination model building procedure. The goodness-of-fit was evaluated with the Hosmer-Lemeshow test, the χ^2 test of the Pearson and deviance residuals and visual inspection of the model residuals.

Comparing post-treatment mortality among centres adjusted for patient case-mix

Post-treatment mortality differences between hospitals were evaluated by estimating their OR adjusted for patient case-mix and displayed in a forest plot relative to the average hospital. Therefore hospital was added as a fixed effect in the Cox regression model. Centres with less than thirty patients were considered to be too small to achieve reliable results and were grouped into a fictitious centre so that their patients could contribute to the estimation of the case-mix covariate regression coefficients. This fictitious centre was not represented in the forest plots.

Clustering of patients into hospitals

Patients from the same hospital, their treatment, care or outcomes can be considered as correlated. In order to account for this clustering of patients into hospitals, hospital was added as a random term to the logistic regression model, unless hospital was added as a fixed effect for comparing centre performance.

Association between post-treatment mortality and centre volume

To evaluate the association between post-operative and post-RT mortality and centre volume, volume was treated as a continuous covariate in the logistic regression model. A plot of the deviance residuals of the model containing all adjustment variables (but not volume) versus centre volume was inspected to decide on the functional form of volume. Linear associations with volume were used.

3.3.4.3 Survival analysis

ESTIMATION OF OBSERVED AND RELATIVE SURVIVAL

Observed survival (OS) proportions were estimated using the Kaplan-Meier method.[42] Relative survival was calculated as the ratio of the observed survival and the expected survival for a similar group of persons from the general Belgian population (stratified on gender, age, calendar year and region). The Ederer II method was applied to estimate the expected survival using the Belgian national lifetables.[43]

The date of diagnosis was taken as time origin. The day of surgery or the date of last RT fraction was used as time origin for the post-treatment survival analyses.

MODELLING OF OBSERVED SURVIVAL

General modelling strategy

The survival over the 0-5 year time interval was modelled with Cox proportional hazards models. Patients surviving beyond 5 years were censored at 5.05 year. Non-proportional hazards between the levels of categorical covariates were evaluated in a univariate way. Detected non-proportional hazards were resolved with a 'piece-wise proportional hazards model' (i.e. proportionality assumption holds within consecutive time intervals). This implies that the follow-up time is split into subintervals, in each interval proportional hazards are assumed. So in each subinterval, a HR was estimated that is assumed to be constant over that interval. A split at one year for example results in two time intervals, [0,1] and [1,4], both with their specific estimated HR.

Then all covariates were combined in the Cox model, including their non-proportional hazard terms. Non-proportional hazards terms that became no longer significant were dropped.

Second order interactions between the main terms were evaluated in a backwards elimination model building procedure. The model assumptions were evaluated on the basis of Schoenfeld and generalised Cox-Snell residuals.

The same baseline patient case-mix variables as for the post-treatment mortality were taken into account (i.e. gender, age group at diagnosis, WHO performance status, combined stage, anatomic site, Charlson Comorbidity Index (CCI) adapted and number of previous inpatient bed days).

Comparing observed survival among centres adjusted for patient case-mix

Survival differences between hospitals were evaluated by estimating their HR adjusted for patient case-mix and displayed in a forest plot relative to the average hospital. Therefore hospital was added as a fixed effect in the Cox regression model. Centres with less than thirty patients were considered to be too small to achieve reliable results. Also in these analyses, small centres were grouped into a fictitious centre so that their patients could contribute to the estimation of the case-mix covariate regression coefficients. This fictitious centre was not represented in the forest plots.

Comparing observed survival between treatment groups

This retrospective observational study does not allow a causal comparison of treatment types, as treatment is not a baseline characteristic and patients are classified on the basis of the treatment they effectively received. Comparing survival in observational studies between patient groups with group definition based on the treatment received is hampered by the so called 'immortal time bias'. As a patient assigned to a treatment group has at least survived long enough to receive this treatment, the patient is as a consequence 'immortal' from time zero up to the moment of (the end of) the treatment. Immortal time bias can artificially increase the survival proportion in the Kaplan-Meier curve, as each patient is not at risk to die during the first part of the study. Immortal time bias was taken into consideration when comparing survival between patients with primary surgery to that of patients with primary RT by considering treatment status as a time-varying covariate. Surgery patients were 'immortal' up to the day of surgery, and RT patients up to the day of their last RT session.

Clustering of patients into hospitals

Also in the survival analyses, the clustering of patients into hospitals was taken into account by adding hospital as a random term to the regression model (as was done in the modelling of post-treatment mortality).

Association between observed survival and centre volume

To evaluate the association between observed survival and hospital volume, volume was treated as a continuous covariate in the Cox regression model. A plot of the Martingale residuals of the model containing all adjustment variables (but not volume) versus hospital volume was inspected to decide on the functional form of volume. Linear or piecewise linear associations consisting of two intervals and both linear sections joined at the knot versus volume were used. When a piecewise linear model was considered, a range of plausible values for the knot was compared and the one giving the lowest AIC (Akaike Information Criterion) was selected for the final model.

The regression model results are visualised by plotting the relation of the predicted HR as a function of hospital volume. The construction of these graphs requires one arbitrary reference choice: which volume is given a HR=1. This choice was guided by the final model.

As an initial step the four anatomic sites were pooled for the volume analysis, then each of the subsites was considered separately with its site-specific volume. When a significant association was observed for the pooled result, HR estimates between anatomical sites (when all HNSCC were considered) and combined stages (for all HNSCC and the anatomical site subgroups) were calculated by adding an interaction between volume and anatomical site or combined stage.

3.3.4.4 Statistical software

Statistical analyses were performed with SAS 9.3 (SAS Institute, Cary, NC, USA). Figures visualising the main treatment volume cox regression results were created with R version 3.4.2.[44]

3.3.5 Case-mix adjustment

When treatment outcomes between providers (e.g. oncologists, surgeons, radiation oncologists or more globally hospitals) who treat patients with different patient and tumour characteristics are compared, case-mix adjustment is certainly indicated. Without adjustment for case-mix, reports and ratings of hospital care may be misleading.[45] Therefore, it is particularly important to capture as many confounders as possible in the analyses, in particular when measuring quality of care and benchmarking hospitals.

3.3.5.1 Patient and tumour characteristics

Factors that are commonly included in risk adjustment models for cancer outcomes include **patient age at diagnosis, gender, anatomic site, and stage of the disease**.

Performance status is an important patient factor that is likely to be associated with the types of treatment that are appropriate, as well as the prognosis.[46] One measure of performance status is the Eastern Cooperative Oncology Group Performance Status (ECOG PS), which has been adopted by the World Health Organization (WHO).[47] While performance status is not directly a comorbidity score, it is a well validated tool for the assessment of fitness for treatment.[48] This score ranges from 0 (asymptomatic, fully active) to 5 (dead). Intermediate scores are 1 (symptomatic but completely ambulatory), 2 (symptomatic, up and about more than 50% of waking hours), 3 (symptomatic, confined to bed or chair more than 50% of waking hours) and 4 (completely disabled; totally confined to bed or chair).

The BCR project database includes the following **patient and tumour characteristics**:

- Age at diagnosis, categorized as follows: <50 years, 50-59 years, 60-69 years, 70-79 years, 80+ years;

- Gender;

- WHO performance status score (ECOG PS), limited to scores 0 to 4;

- Clinical, pathological and combined TNM stages according to the 6th version of the TNM (incidence year 2009) or the 7th version of the TNM (incidence years 2010-2014);[38, 39]

- Anatomic site (RARECAREnet definition layer 2; see Appendix 1) (i.e. oral cavity, oropharynx, hypopharynx and larynx).

3.3.5.2 Patients' comorbidities

INTRODUCTION

In addition to the patient and tumour characteristics described above, the survival of patients with head and neck squamous cell carcinoma (HNSCC) also depends on the aggressiveness of the primary cancer, patient's comorbidities[49] and patient related risk factors, such as smoking,[50-53] alcohol abuse,[53-57] but also infection by HPV (Human PapillomaVirus).[54, 58, 59] These risk factors contribute to HNSCC as well as to other diseases, including cardiovascular, pulmonary or hepatic diseases, that may co-exist with the diagnosed cancer and are called comorbidities.

Comorbidity is described as the presence of one or more medical conditions (physical or mental diseases), next to the primary tumour but not caused by the primary tumour. Such diseases are already present at the time of diagnosis of HNSCC and may affect the ability of patients to function, may influence therapeutic decisions and the patient's tolerance to treatment, but may also have an impact, whatever their severity, on the outcomes (short-term mortality and long-term survival).[49, 60-65] Therefore, it is meaningful to take comorbidity data into account when comparing patients' outcomes between hospitals within one country and between countries based on population-based data.

Measuring comorbidities in cancer populations is complex, and no gold standard approach exists.[66] Ideally, in a population-based study, the presence of comorbid diseases at diagnosis should be assessed by a standardized clinical evaluation for each patient, and data need to be systematically recorded. However, this evaluation needs to be planned (prospectively) and is costly and time consuming. An alternative solution to minimize costs and obtain estimations about the presence of comorbid

conditions of the patients, is to use administrative data from hospital registries (e.g. hospital discharge data). In the present study we applied the latter approach, using the hospital discharge data (MZG – RHM data, see section 3.1.3).

VALIDATED INSTRUMENTS TO MEASURE COMORBIDITY IN HNSCC PATIENTS

There are several validated instruments designed to code and quantify comorbidity in patients including the Washington University Head and Neck Comorbidity Index (WUHNCI), National Cancer Institute Comorbidity Index, Head and Neck Cancer Index (HNCA), Elixhauser – van Walraven point score, the Cumulative Illness Rating Scale (CIRS), the Kaplan-Feinstein Index (KFI), the Charlson Comorbidity Index (CCI) and its variants, the Index of Coexistent Disease (ICED), the Adult Comorbidity Evaluation 27 index (ACE-27). These instruments require data on different comorbidities, collected prospectively or retrospectively from the patient's medical file or from administrative databases.

The Clinical Comorbidity Index developed by Charlson[67] is one of the most used method of categorising comorbidity to predict short- and long-term mortality from medical records.[50, 68-71] For this reason and after discussion with the clinical experts about the measurability of different indexes using hospital discharge data, the CCI was chosen for this study.

THE CHARLSON COMORBIDITY INDEX (CCI)

Background

The Charlson Comorbidity Index uses the primary and secondary diagnoses registered for each hospital admission before and around diagnosis, taking into account the following diseases: myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, dementia, chronic pulmonary disease, rheumatic disease, peptic ulcer disease, mild liver disease, moderate or severe liver disease, diabetes without chronic complication, diabetes with chronic complication, renal disease, hemiplegia or paraplegia, any malignancy (including lymphoma and leukaemia, except malignant neoplasm of skin), metastatic solid tumour and AIDS/HIV. The original CCI has been adapted for administrative databases and the

corresponding codes for diagnoses and procedures (ICD-9-CM) are now available.

Later on, several authors proposed additional adaptations, including extra comorbidities, to investigate other patient population types (the testing sample in the original study was composed of breast cancer patients followed for ten years from the time of their first treatment) or other outcomes. The two most frequently applied and cited adaptations are the Deyo-Charlson[72] and Romano-Charlson[73] adaptations of the CCI. There are slight differences between both adaptations: Romano's adaptation includes a larger number of comorbid conditions than the Deyo version.[74, 75] Several authors compared and evaluated the performance and predictive power of both and came to the conclusion that the Romano-Charlson version was slightly superior in predicting short- and long-term mortality.[76-78]

Adaptation of the Romano-Charlson version

As it is suggested in the international literature, we chose to use the Romano-Charlson version of CCI. However, subsequent studies investigated coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative databases.[68, 71] Interestingly, Quan et al. (2005)[71] developed new coding algorithms of which the coverage of comorbidities was slightly better than the existing algorithms. A pre-test of the adjusted algorithms in the MZG-RHM database, indeed resulted in a better capture of two comorbidities in our sample (i.e. rheumatologic disease and mild liver disease). As a consequence, two codes were added, respectively polymyalgia rheumatica in the rheumatologic disease group (ICD-9-CM code 725) and chronic hepatitis in the mild liver disease group (ICD-9-CM code 571.4-571.49).

Additionally, because only patients with unique tumours were selected for the study, no patient will present a comorbidity belonging to the category 'Any malignancies, including leukaemia and lymphoma'. The final list of codes used for the construction of the Romano-Charlson score is presented in Table 56 in Appendix 4, coupled with their respective weights.

The comorbidity index was calculated based on all hospital discharge data available for each patient from '1 year preceding the start of the treatment for HNSCC' to (and including) 'the stay during which the first treatment was delivered for HNSCC'. In case no cancer treatment was recorded, the incidence date was considered as reference date (Table 3).

Since the Romano-Charlson version considers two categories (severities) for liver disease and diabetes, it is possible that for one patient two different ICD-9-codes are registered in the hospital discharge data (MZG – RHM data) during the time frame under consideration (e.g. once diabetes without chronic complications and once diabetes with chronic complications). As both codes correspond to different weights, which cannot be added up, it was chosen to only select the ICD-9-code that was registered closest to the reference date (i.e. start date of first treatment or incidence date when there was no cancer treatment). In exceptional cases, two codes (hence, different levels of severity) were identified on the same day; in these cases we opted for the most severe form.

A feasibility study was conducted to calculate the Romano-Charlson score using the linked MZG – RHM database and BCR database (see section 3.1.3 for more details). Table 3 shows the availability of hospital discharge data for HNSCC patients, by anatomic site and for the whole sample.

Table 3 – Availability of hospital discharge data for patients diagnosed with HNSCC (2009-2014)

	Oral cavity	Oropharynx	Hypopharynx	Larynx	Total
	2 665	**2 745**	**1 137**	**2 698**	**9 245**
Number of patients with at least one hospitalization reported in MZG – RHM data:	2 630 (98.7%)	2 724 (99.2%)	1 130 (99.4%)	2 690 (99.7%)	9 174 (99.2%)
• **The year preceding the reference date* (stay during which first treatment was given, is excluded)**	2 094 (78.6%)	2 330 (84.9%)	1 018 (89.5%)	2 379 (88.2%)	7 821 (84.6%)
If not (all exclusive),					
• **The stay during which the first treatment was given**	301 (11.3%)	132 (4.8%)	9 (0.8%)	77 (2.9%)	519 (5.6%)
• **The week after the first treatment was given**	9 (0.3%)	16 (0.6%)	3 (0.3%)	8 (0.3%)	36 (0.4%)
• **Outside the predefined time frames**	226 (8.5%)	246 (9.0%)	100 (8.8%)	226 (8.4%)	798 (8.6%)
Number of patients with no hospitalization reported in MZG – RHM data	35 (1.3%)	21 (0.8%)	7 (0.6%)	8 (0.3%)	71 (0.8%)

* Reference date: for patients who received cancer treatment this is the start date of treatment, for the remaining patients this is the incidence date.
Source: BCR – IMA – MZG

A macro was created in SAS® (SAS software 9.4) to assign to each patient a Romano-Charlson comorbidity score, which was included in the analyses as a categorical variable (0 points, 1 or 2 points, 3 or 4 points and >4 points).

When in the report 'Charlson Comorbitity Index adapted' is written, this should be read as: 'the Charlson Comorbitity Index after adaptation as is described in section 3.3.5'.

3.3.5.3 Previous inpatient bed days

Another parameter that can be taken into account in case-mix adjustment is the number of bed days of hospitalisation preceding the diagnosis of cancer.[79] In the present study the **number of days spent in a hospital** by the patient within twelve months before start date of cancer treatment (or incidence date when no cancer treatment was performed) was included in the analysis as a categorical variable (no days, 1-5 days, 6-15 days and more than 15 days).

When in the report 'previous inpatient bed days' is written, this should be read as: 'the number of days spent in a hospital by the patient within twelve months before start date of cancer treatment as is described in section 3.3.5'.

3.3.5.4 Final remarks on case-mix adjustment

None of the available databases (BCR, IMA – AIM, MZG – RHM) contained data on other well-established confounding factors, like HPV infection, the socio-economic background of the patient, alcohol consumption and smoking.[80-84] A better proxy than the Charlson Comorbidity Index, which includes some pathologies that are also associated with alcohol consumption and smoking (e.g. peripheral vascular disease, chronic pulmonary disease, liver disease), was not possible.

3.4 Step 4: Assignment of each patient to one centre

For the benchmarking between hospitals, the volume – outcome analyses as well as the individual feedback to the hospitals, each patient had to be assigned to one centre, also when a patient was taken care of in more than one hospital. For that purpose, the RIZIV – INAMI licensing codes mentioned in the IMA – AIM database were used to identify the hospital where a procedure took place. Fusions between hospitals were taken into account until the end of 2014, the last included incidence year of the study.

Depending on the quality indicator under assessment, assigning the patients to a hospital was done based on the centre of main treatment, the centre of first treatment, the centre of surgery, the centre of radiotherapy or the centre of diagnosis. Therefore, several assigning algorithms were constructed.

Centre of main treatment

In order to define the centre of main treatment, several diagnostic and therapeutic procedures performed during the predefined time frames (cf. section 1.1.1) were taken into account: surgery with curative intent, radiotherapy with curative intent, systemic treatment, biopsy and the multidisciplinary team meeting (MDT). Palliative RT was not taken into account to define the centre of main treatment.

Algorithm for main treatment allocation (Between brackets: the cumulative percentage of assigned patients per rule):

1. If all available procedures mentioned above (except biopsy) occurred in the same centre, that centre was chosen as the centre of main treatment (63%);

If the patient underwent procedures in different centres, the following rules applied:

2. If the main treatment was surgery, the centre of surgery was selected (73%);

3. If the main treatment was radiotherapy (with or without systemic therapy), the centre of radiotherapy was selected (97%);

4. If the main treatment was systemic therapy only, the centre of systemic therapy was selected (97%);

5. If no treatment was identified, the centre of biopsy was selected (99%).

For a very small number of patients, the centre of main treatment was unknown based on IMA – AIM data. For these patients, the following priority rule was applied. For example, when the treatment scheme was surgery but the centre of surgery was unknown in IMA – AIM data, the centre of radiotherapy was selected. When the patient did not undergo radiotherapy, the centre of systemic therapy was selected, etc.

Centre of first treatment

For the centre of first treatment, surgery with curative intent, radiotherapy with curative intent and systemic therapy were taken into account when performed during the predefined time frames (cf. section 1.1.1). The centre where the first of these treatments was performed, was selected as the centre of first treatment. Based on this rule 92% of the patients could be assigned a centre of first treatment. For an additional 6% of patients the centre of first treatment was attributed based on the hospital where the biopsy took place.

Centre of surgery with curative intent

The centre of surgery with curative intent was the centre where the selected surgery with curative intent took place within the predefined time frames (see also section 3.3.2); the centre of surgery could be assigned to 99.8% of patients who had surgery with curative intent as primary treatment.

Centre of radiotherapy with curative intent

When radiotherapy with curative intent was performed within the predefined time frame, the centre where this radiotherapy was performed was selected. In case patients received RT in two different RT centres, the centre where the first RT was given was selected. The centre of RT could be assigned to 99.9% of patients who had RT with curative intent as primary treatment.

In Belgium there are 25 'main radiation oncology departments' and 11 'satellite radiotherapy units' (which are affiliated with one of the main centres). However, based on the RIZIV – INAMI licensing codes mentioned in the IMA – AIM database, the distinction between both cannot be made. Hence, all patients who had RT with curative intent were assigned to one of the main RT centres.

Although the number of main radiation oncology departments is limited to 25, 26 RT centres were identified in the database. The reason is that one department closed on 31 December 2014 and another opened on 1 January 2015.

Centre of systemic therapy

The centre of systemic therapy could be either the centre where chemotherapy was given, or the centre where targeted therapy was given. When targeted therapy and/or chemotherapy were given in more than one centre, the centre where the first systemic therapy was delivered, was selected. Only systemic therapy performed within the predefined time frame was taken into account to define the centre. The centre of systemic therapy could be assigned to 98.6% of patients.

Diagnostic centre

The diagnostic centre was defined as the centre where the biopsy was performed (see Appendix 3.1.5). The centre of biopsy could be determined for 89% of the patients. If no centre of biopsy could be identified, the centre of the first treatment was taken into account (see above). For an additional 10% of patients, the centre of first treatment was added. Only biopsies performed within the predefined time frame were taken into account to define the centre of diagnosis.

3.5 Step 5: Validation of diagnostic and therapeutic data

3.5.1 Introduction and methodology

As was explained in section 3.1, calculation of quality indicators of care for squamous cell carcinoma of the head and neck is based on the linkage of Belgian Cancer Registry data (BCR data) and administrative data (financial claims data) from the health insurance companies (IMA – AIM data). Because it remains impossible to unambiguously link the health insurance data to a (cancer) diagnosis, a subproject was initiated to validate the data and methodology used to identify diagnostic and therapeutic procedures that are needed to calculate the quality indicators. The main research question of the validation project was '*Is it possible to correctly identify diagnostic and therapeutic procedures for HNSCC patients using BCR data linked to health insurance data and can patients correctly be assigned to one treatment hospital?*' Data that are available at the hospital (e.g. medical files, financial data…) are used as the gold standard in this project.

Upfront, it was decided that a deviation of 5% would be considered as acceptable.

A diverse sample of sixteen hospitals was selected for this validation process, taking into account academic versus non-academic hospitals, the (preliminary) average annual HNSCC treatment volume of the hospitals (high: >50 patients; medium: 20-50 patients; low: <20 patients) and their geographical location. Four hospitals refused to participate in the validation project or did not respond (even after having sent reminders), hence four

comparable hospitals were invited to participate. The list of participating hospitals is provided in the Appendix 5.1.

The number of patients to be checked by the different hospitals depended on the volume of the hospital: 2 high-volume hospitals checked the data of around 100 patients, 4 medium volume hospitals of 45 to 60 patients and 10 low-volume hospitals had a maximum of 25 patients to validate. Each hospital received a list of patients with HNSCC diagnosed between 2004 and 2013, who were assigned to the hospital using a proposed algorithm to assign patients to one treatment hospital (see Appendix 5). The information provided to the hospitals for each assigned patient and the checks asked to be done are provided in Appendix 5.3

For hypopharynx and larynx, only T3 and T4 (clinical-T prevails over pathological-T) tumours were included because a pre-investigation with six hospitals revealed that for small tumours in these anatomic sites it was not possible to differentiate surgical procedures with curative intent from diagnostic procedures.
The number of incidence years to be validated depended on the volume of the hospital, but the year 2013 was included for each hospital.

The results of the validation process were anonymously presented to the participating hospitals (during a dedicated meeting) and thoroughly discussed (anonymously) with the clinical experts.

3.5.2 Validation of the algorithm to assign patients to one treatment hospital

Hospitals were asked to validate the correctness and completeness of the list of patients assigned to their hospital for the incidence year 2013 only. Hospitals were asked not only to validate the listed patients (ranging from 1 to 104 patients per hospital), but also to look for additional patients that were incorrectly not assigned to them by the BCR.

3.5.2.1 Results

Overall, 371 of the total number of 384 patients (97%) were correctly assigned to the treatment hospital, with a range of 84% to 100% of patients over the different hospitals. Hospitals with the lowest percentages of correctly assigned patients were hospitals with less than ten patients assigned to them for the incidence year 2013. More details on correctness and completeness of the patient lists can be found in Appendix 5.4.

An important remark from the participating RT centres was, that based on the algorithm that was used, many patients who were referred to them for RT were not assigned to their centre, but to the centre where e.g. chemotherapy was given. This resulted in a lower volume for these RT centres. As a consequence the assignment algorithm was, after discussion with the clinical experts, changed (cf. infra).

3.5.2.2 Conclusion

The overall quality of the assignment algorithm was considered good. However, correctly assigning patients to a hospital strongly depends on the exhaustiveness and quality of the data delivery to the cancer registry (e.g. anatomic site, TNM staging…). Additionally, misclassifications and non-specific nomenclature codes for medical procedures in the IMA – AIM data are barriers to optimally identify the treatment scheme of HNSCC patients and to assign each patient to one treatment hospital.

The validation phase resulted in a very important change in the assignment algorithm, which was suggested by the participating hospitals and confirmed by the clinical experts. More precisely, a higher priority was given to the centre where radiotherapy was performed: patients receiving primary chemoradiotherapy were assigned to the radiotherapy centre (Appendix 5.4, Table 57).

3.5.3 Validation of patient and tumour characteristics and of diagnostic and therapeutic procedures as identified in the health insurance data linked to cancer registry data

Each of the sixteen hospitals received a list of patients assigned to their hospital, ranging from 15 to 104 patients per hospital and a total number of 602 patients for the sixteen hospitals together. The included incidence years depended on the hospital's volume; they were selected from the time frame 2004-2013.

3.5.3.1 Results

The results are described in detail in Appendix 5.5 (patient and tumour characteristics) and Appendix 5.6 (diagnostic and therapeutic procedures).

3.5.3.2 Conclusions

The validation phase revealed some important issues which were (whenever possible) tackled in order to further optimize the methodology of the project.

First of all, the results showed that the **tumour characteristics** in the cancer registry database are not always complete or correct. However, not all inconsistencies would have an impact on the calculation of quality of care indicators, e.g. small deviations in the incidence date, corrections in topography with no change of the anatomic site, and change of the histological subtypes of SCC of the head and neck do not directly influence the results of the study. Inconsistencies with an actual impact on the calculation of quality indicators were limited and remained within an acceptable level inherent to population-based studies. Reported changes in the clinical and pathological stage of the tumour concerned most of the time completion of missing information. Since the in- or exclusion criteria for the denominators of most quality of care indicators are based on staging information, patients with missing staging information are not included in the calculation of those indicators. This does not necessarily mean that the results are incorrect, but a certain level of bias cannot be ruled out as it is very well possible that patients with missing staging information would score differently from their peers with complete staging information. Inconsistencies in the staging information that change the classification into

small (T1,2,x) versus large (T3,4) tumours could not only impact the in- or exclusion for quality indicators, but also the definition of surgery with curative intent (see section 3.3.2), or even the in- or exclusion in the validation phase for SCC of the hypopharynx and larynx. A change in the regional lymph node status or distant metastasis also influences the in- or exclusion criteria for some quality indicators, but according to the experts the number of such changes could be considered acceptable. Though, the results of the validation study illustrate clearly that more efforts are required to further improve the quality of data delivered to the cancer registry for future projects, especially for staging information.

The results related to **diagnosis and staging information** seem to be good for **CT-scan**, **biopsy** and cytology of the primary tumour. No changes to the nomenclature selections for these procedures were indicated. Overall results for the discussion of patients on the **MDT** in general and for MRI in patients with SCC of the oropharynx were underestimated based on available data for the BCR and neared the boundary of acceptancy for the project. Already in previous projects on quality indicators it has been shown that more patients are discussed during an MDT than what could be identified in IMA – AIM data, mainly caused by billing rules. The number of MDTs that can be billed per patient is limited to one per year, while in reality many patients are discussed several times a year during an MDT. In case the one MDT that is invoiced falls outside the defined time frame for the study, it is not captured for the study and others (which may have fallen within the time frame) are not recorded in the IMA – AIM database. In addition, misclassifications can never be ruled out when working with administrative data. With this in mind, it was decided to give less importance to the centre where the MDT took place in the algorithm to assign patients to a hospital. For **MRI** of the primary tumour in patients with oropharyngeal and oral cavity SCC, it was deduced from the validation phase that exclusion of nomenclature code 459395/459406 (upfront considered as intended for the assessment of metastases) in fact resulted in a substantial underestimation of the number of patients with an MRI of the primary tumour, hence the nomenclature code was included for oropharyngeal and oral cavity SCC in the main study.

Furthermore, the inclusion of **patients with multiple tumours** created problems because the nomenclature codes cannot directly be linked to the exact diagnosis. Especially when multiple tumours in one patient are diagnosed and/or treated in the same time period, medical procedures can erroneously be taken into account for another tumour. Experts decided that it would be more straightforward to exclude patients with multiple tumours from the project, in order to increase the probability that the identified medical procedures were indeed performed for a HNSCC. Yet, the inclusion of procedures for non-oncologic reasons remains possible, but probably at a very low rate.

There is only limited difference in the overall results (for all hospitals together) for **surgery with curative intent** when comparing the use of available data from the BCR with the data of the hospital; for all anatomic sites this difference stays within the limits of 5%. However, at the individual patient level there are more inconsistencies. The majority of them in SCC of the oral cavity are caused because of unspecific nomenclature codes, where it is often unclear whether they are used for procedures with a diagnostic purpose or with curative intent. Based on the validation procedure, it was decided to further exclude the nomenclature codes 310914/310925, 311135/311146 and 353231/353242 for the definition of surgery with curative intent for oral cavity tumours because they were responsible for false positive results. Excluding them caused less problems than including them.

The way **lymphadenectomy** was taken into account in the algorithm to define surgery with curative intent (see section 3.3.2) caused some problems of erroneously selecting lymphadenectomy without a nomenclature code for surgery with curative intent as surgery for the primary tumour. This problem could be resolved in the majority of cases by no longer taking lymphadenectomy performed after radiotherapy into account to define surgery with curative intent. Other inconsistencies could not be resolved without causing more problems, but the clinical experts agreed that errors were reduced to an acceptable level. Results for **reconstructive surgery** were good, with no demand for adaptations.

Although some errors were observed for radiotherapy and chemotherapy, half of them were induced by an error in the definition of surgery with curative intent and could partly be resolved by refining the definition of surgery with curative intent, as described above. Another large part of errors in radiotherapy were due to a programming error, which was corrected before the start of the main study. The algorithm used by the BCR to estimate the start date of radiotherapy proved to be a good approach of the real start date. Based on the results of the validation, the products Celecoxib and Purinethol were excluded for the main study because they are not used in the context of treatment of SCC of the head and neck.

Although the overall results obtained from the administrative IMA – AIM data linked to cancer registry data did not differ more than 5% from the overall results obtained from hospital data, the differences in individual hospitals can be quite large for almost all medical procedures under investigation. Especially in low-volume hospitals this difference can be very large, because a change for a very limited number of patients (sometimes only one patient) can cause enormous fluctuations in the proportional results.

After thorough discussion of the results, the clinical experts agreed to accept the remaining larger differences at the individual hospital level and to continue with the calculation of the quality of care indicators, as it is probably so far the most optimal methodology to near reality, based on readily available data in Belgium. Though, cautiousness is needed in interpreting the results on the individual hospital level.

Based on the results of this validation phase, the methodology was optimized and the database updated, also including incident cases from the year 2014 (which were not yet available at the time of the validation phase). The technical fiches and analysis methods were agreed and finalised before the analyses were started.

3.6 Step 6: Measurement of quality indicators, at national level and by centre

All selected QIs were measured at a national level and by treatment or diagnostic centre, where considered appropriate. All analyses were performed by the BCR team (see co-authors with BCR-affiliation).

3.7 Step 7: Interpretation of results

The results were thoroughly discussed with the expert panel. Based on the results, recommendations for quality improvement were formulated and further discussed with stakeholders (see colophon).

4 CHARACTERISTICS OF THE STUDY SAMPLE

In the present chapter a description is given of the baseline patient and tumour characteristics of the 9 245 patients diagnosed with a squamous cell carcinoma of the head and neck in 2009-2014, who were included in the present study. In addition a brief description is given of the main diagnostic, staging and therapeutic procedures that were recorded for these patients.

4.1 Baseline demographics and tumour characteristics

4.1.1 Patient characteristics

Head and neck squamous cell carcinoma (HNSCC) occur more frequently in men (75.9%) than in women. The mean age at diagnosis was 62.3 years. According to the WHO performance status, the majority of patients was asymptomatic (WHO = 0; 16.9%) or symptomatic but completely ambulatory (WHO = 1; 62.4%) at the time of diagnosis. For 8 812 patients of the total study population, hospital discharge data of the year preceding cancer treatment (or preceding incidence date when no cancer treatment was given) were available and were used to estimate comorbidities and calculate the Adapted Charlson Comorbidity Index (see section 3.3.5). Most prevalent comorbidities were chronic pulmonary disease (19.4%), diabetes without chronic complications (8%) and peripheral vascular disease (5.6%). Yet, 60.8% of the 8 812 patients had no comorbidities. More details on patient characteristics of both the total study population and the four anatomic sites are presented in Appendix 6.1, Table 78.

4.1.2 Tumour characteristics

Because clinical stage (c-stage, Figure 2) was missing in the BCR database for 19.5% of the included patients and pathological stage (p-stage, Figure 3) was missing for 21.6% of patients who received surgery, a combined stage was calculated for each patient (Appendix 6.1, Table 79). To determine this combined stage, known p-stage prevailed over known c-stage, except when there was clinical proof of distant metastasis. When only the c-stage was known, this stage determined the combined stage. Obviously, when neither the p-stage nor the c-stage were known, the combined stage was unknown too, which was the case for 10.8% of the patients. Note that a tumour with a missing stage can be both a tumour for which the stage was not reported to the BCR, as well as a tumour for which the stage was unknown or could not be defined. The interested reader will find more details on stage reporting in section 5.1.3 where the quality indicator 'Proportion of patients with HNSCC who have their cTNM and pTNM stage reported to the Belgian Cancer Registry' is fully elaborated.

Two thirds of the patients with known stage were diagnosed with an advanced stage of the tumour (cIII-IV, 66.7%). However, as is presented in Figure 2, this proportion varied considerably among the different anatomic sites: from 46.5% for laryngeal SCC to 89.9% for hypopharyngeal SCC (Appendix 6.1, Table 79). For all HNSCC patients who had surgery and for whom the pathological stage was reported to the BCR, pathological stage I and IVA were most common (32.8% and 35.6% respectively, Appendix 6.1, Table 79). However, for hypopharyngeal SCC the results were different with only 7.3% of patients for whom a p-stage I was recorded and 68.5% of patients with a p-stage IVA (Figure 3 and Appendix 6.1, Table 79). Last but not least, when interpreting these data, one has to keep in mind that the pathological stage can refer to any pTNM, for instance also a pathologic staging performed after neoadjuvant therapy (ypTNM), which may have resulted in downstaging.

Figure 2 – Distribution of clinical stage by anatomic site (HNSCC, incidence 2009-2014)
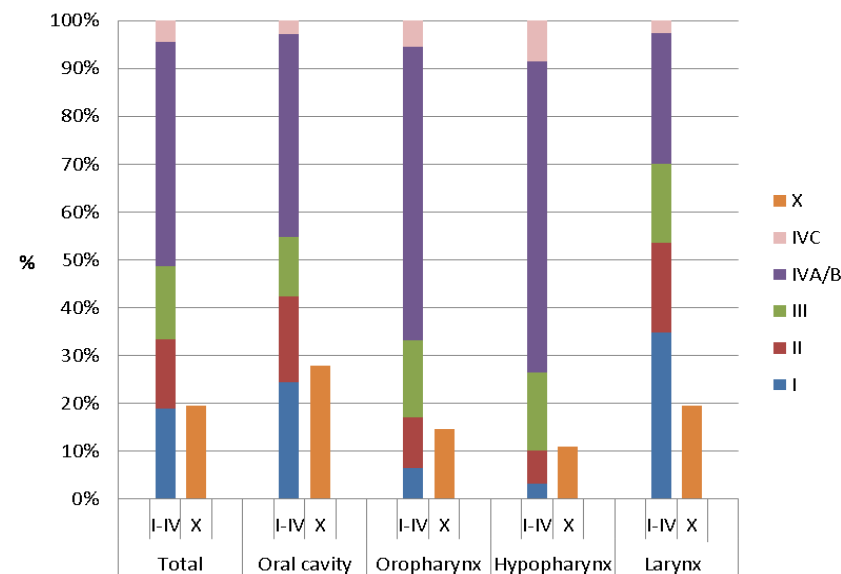
Source: BCR

Figure 3 – Distribution of pathological stage by anatomic site (HNSCC, incidence 2009-2014)
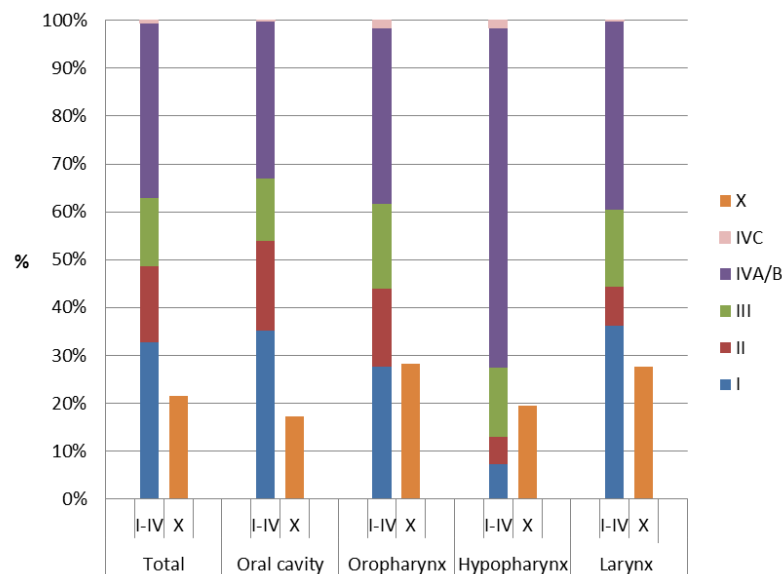
Source: BCR – IMA

Consistency between clinical and pathological stage was evaluated for those patients who underwent surgery, and for whom both clinical and pathological stage were reported to the BCR. The analyses revealed that the pathological stage was identical to the clinical stage for 784 patients (i.e. 66.4% of 1 181 eligible patients) with an oral cavity SCC (Appendix 6.1, Table 80), for 218 patients (i.e. 61.8% of 353 eligible patients) with an oropharyngeal SCC (Appendix 6.1, Table 81), for 87 patients (i.e. 82.1% of 106 eligible patients) with a hypopharyngeal SCC (Appendix 6.1, Table 82), and for 320 patients (i.e. 72.9% of 439 eligible patients) with a laryngeal SCC (Appendix 6.1, Table 83).

4.2   Main diagnostic and staging procedures

An overview of the most common diagnostic and staging procedures in the diagnostic work-up of HNSCC patients is reported in Table 84 (Appendix 6.2); after discussion with the clinical experts, it was decided to limit the time span for evaluation to three months before and three months after the incidence date [d].

A **multidisciplinary team meeting** [e] (MDT) was recorded for 82.3% of the total study population; the lowest percentage was recorded for patients with a SCC of the oral cavity (77.7%, Appendix 6.2, Table 84). The interpretation of these data should be done with caution: besides the fact that we are dealing with administrative data (with the inherent limitations), MDT data require special attention since special financing rules apply, which also changed during the time span of the study period.[85] For instance, before 1 November 2010 only one MDT per calendar year was reimbursed which implies that other possible MDTs were not registered in the IMA database.[85] Even then, these financing rules cannot fully explain why for 1 637 patients [f] (18% of the study population) no MDT was recorded within the given time frame.

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[d]   The way the incidence date is defined in the present study, is explained in section 3.1.1.

[e]   All MDT related nomenclature codes (e.g. for first, follow-up and additional MDT) were taken into account.

[f]   Of the total group of 1 637 patients who did not have an MDT within the time frame, 708 were referred patients (i.e. in whom the treatment was given in a different centre than the centre where the biopsy took place), 666 patients received treatment in the centre of biopsy and for 263 patients it was not possible to define (based on the administrative data) their referral status.

Imaging is not only important in the diagnostic phase of HNSCC, but also in the development of a treatment plan. The most frequent imaging exams performed were CT of the neck (92.5%) and RX of the thorax (73.3%). An MRI of the neck was performed in 30.1% of the cases; ranging from 19.3% in laryngeal SCC to 37.7% in oropharyngeal SCC patients. PET(/CT) was performed in 47.9% of the total study population, again with an obvious difference between different anatomic sites (36.0% in laryngeal SCC versus 62.3% in hypopharyngeal SCC).

The most commonly performed **endoscopic procedure** was tracheoscopy/laryngoscopy (84.9%), which was performed in only 60.0% of patients with oral cavity SCC but in 98.6% of patients with laryngeal SCC. For almost all patients (98.7%), a **biopsy** of the primary tumour was taken.

4.3 Main therapeutic procedures

Half of the HNSCC population was treated with primary radiotherapy (RT), with or without systemic therapy (49.7%) and another large group with surgery with curative intent, with or without (neo)adjuvant therapy (38.1%;Table 4). Clear differences can be seen between the four anatomic sites: while the majority of oral cavity SCC patients (73.4%) received surgery with curative intent and only 15.2% primary RT, the opposite is true for patients with a hypopharyngeal SCC who are predominantly treated with primary RT (69.9%) and to a lesser extent with surgery with curative intent (13.5%). Seven percent of the total study population received only palliative RT (i.e. short course RT) or no cancer treatment.

Table 4 – Main therapeutic procedures (primary treatment) for HNSCC patients diagnosed in 2009-2014

	Total (N=9 245)		Oral cavity (N=2 665)		Oropharynx (N=2 745)		Hypopharynx (N=1 137)		Larynx (N=2 698)	
	N	%	N	%	N	%	N	%	N	%
Surgery with curative intent	3 518	38.1	1 957	73.4	644	23.5	154	13.5	763	28.3
Surgery only	1 748	18.9	1 024	38.4	231	8.4	33	2.9	460	17.1
Surgery < RT	904	9.8	502	18.8	169	6.2	41	3.6	192	7.1
Surgery < SystRT	699	7.6	340	12.8	211	7.7	66	5.8	82	3.0
Surgery < Syst	88	1.0	43	1.6	26	1.0	3	0.3	16	0.6
Syst < Surgery	18	0.2	12	0.5	3	0.1	0	0.0	3	0.1
Syst < Surgery < RT	27	0.3	18	0.7	1	0.0	6	0.5	2	0.1
Syst < Surgery < SystRT	26	0.3	12	0.5	3	0.1	5	0.4	6	0.2
Syst < Surgery < Syst	8	0.1	6	0.2	0	0.0	0	0.0	2	0.07
(Syst)RT < Surgery (< adjuvant treatment)	70	0.8	15	0.6	27	1.0	6	0.5	22	0.8
Primary (Syst)RT (no major surgery)	4 596	49.7	404	15.2	1 724	62.8	795	69.9	1 673	62.0
RT only	1 715	18.6	108	4.1	379	13.81	146	12.8	1 082	40.1
SystRT	2 881	31.2	296	11.1	1 345	49.0	649	57.1	591	21.9
Primary systemic therapy (no major surgery, no radiotherapy)	381	4.1	85	3.2	144	5.3	94	8.3	58	2.2
Chemotherapy only	260	2.8	72	2.7	92	3.4	54	4.8	42	1.6
Chemo-/Targeted therapy	111	1.2	13	0.5	46	1.7	36	3.2	16	0.6
Targeted therapy only	10	0.1	0	0.0	6	0.2	4	0.4	0	0.0
Palliative RT only	13	0.1	4	0.2	3	0.1	2	0.2	4	0.2
No cancer treatment	667	7.2	200	7.5	203	7.4	86	7.6	178	6.6

<: followed by; RT: radiotherapy; Syst: systemic therapy (=chemo and/or targeted therapy; (Syst)RT < Surgery (< adjuvant treatment): based on the nomenclature codes impossible to distinguish induction RT followed by surgery from primary RT followed by salvage surgery; adjuvant treatment can be RT and/or systemic treatment after surgery. Source: BCR – IMA

From the 9 245 studied HNSCC patients, a quarter received both surgery for the primary tumour and a lymphadenectomy; this proportion was highest for the oral cavity SCC cases (53.5%) and lowest for hypopharyngeal SCC (11.4%, Table 85 in Appendix 6.3). Only 13.0% of HNSCC patients received surgery with curative intent for the primary tumour in the absence of a lymphadenectomy. A small proportion (3.9%) only had a lymphadenectomy; the lowest proportion was observed in oral cavity (2.0%) and laryngeal SCC (2.1%) and the highest in the hypopharyngeal SCC group (7.0%).

Further, we also evaluated how the primary treatment of HNSCC patients varied according to the clinical stage; this evaluation was performed by anatomic site. Indeed, in the oral cavity SCC group, the proportion of patients undergoing surgery with curative intent decreases with increasing clinical stage, while the proportion of patients receiving primary (systemic)RT or no cancer treatment increases (Appendix 6.3, Table 86). In patients with oropharyngeal SCC, more than half of the patients with stage I were treated with surgery and one third with primary (systemic)RT, while the reverse can be seen for higher non-metastatic stages (Appendix 6.3,Table 87). Surgery with curative intent was performed more often for patients with clinical stage I or IVA hypopharynx SCC than for other stages, while they were less often treated with primary (systemic)RT than other non-metastatic stages (Appendix 6.3, Table 88). When surgery with curative intent was performed in patients with laryngeal SCC, this was most often for stage IVA tumours (Appendix 6.3, Table 89). Primary systemic therapy was for all four tumour types much more often given for patients with metastatic disease (stage IVC) than for any other stages.
In Appendix 6.4, an overview is presented of the chemotherapy and targeted therapy products used in patients with oral cavity, oropharyngeal, hypopharyngeal and laryngeal SCC (Table 91). After discussion with the experts it was decided that all systemic therapy products given within the time span one month before until six months after incidence date, should be included in the analyses.

HNSCC patients for whom no treatment was identified in the administrative database

Importantly, for 680 (7.4%) HNSCC patients, no cancer treatment could be identified in the database. It is very well possible that this is exactly what happened in reality, for instance because the patient was already too frail at the time of diagnosis, because he died shortly after diagnosis or had a very bad prognosis. Yet, we must realise that in reality some of these patients may have received some kind of treatment, but that this treatment was not recorded well, was given within the scope of a clinical trial (and thus not recorded in the IMA – AIM database) or was confined to palliative/supportive care.

Table 90 in Appendix 6.3 gives an overview of the characteristics of HNSCC patients who received only palliative RT (N=13) or no cancer treatment (N=667). Most of these patients were males (74.4%) and were symptomatic but completely ambulatory (44.9%). Their mean age was 68.5 years and half of them were diagnosed with an advanced stage (III-IV: 50.7%). Interestingly, for one third of these patients no clinical stage was reported to the BCR. Forty-six percent of this patient group had died within three months after incidence date and another 11.2% within six months of the incidence date. The median survival length after diagnosis was 108 days. Almost half of them (49.6%) had at least one comorbidity.

4.4 Time trends for main diagnostic, staging and therapeutic procedures

Although the study population was confined to those patients with a HNSCC diagnosed between 2009 and 2014, it was believed that for some diagnostic, staging and therapeutic procedures it could be informative to present some trends over a longer time period (as BCR has data from 2004 onwards); the time trends for HNSCC with incidences between 2004 and 2014 for diagnostic and staging procedures are visualized in Figure 25 (Appendix 6.5). Those for therapeutic procedures are given in Figure 26 and Figure 27 (Appendix 6.5).

From these time trend analyses it is apparent that the proportion of patients discussed during an MDT has increased substantially over time for the four SCC types (Appendix 6.5, Figure 25). Over time, an RX of the thorax was less frequently performed (a decrease of 10 to 20% over the eleven year time span), while the use of a CT of the neck was quite steady. The proportion of patients for whom a CT of the skull was performed remained more or less stable over the years. Since 2004, the use of an MRI has increased for oropharyngeal and oral cavity SCC while it remained relatively stable for hypopharyngeal and laryngeal SCC. The use of a PET(/CT) scan has increased substantially during the period 2004-2014 for all anatomic sites. The use of an ultrasound of the neck remained quite stable (and low) over time, while an ultrasound of the abdomen has decreased with about 20% over time.

While in 2004 nearly 65% of oral cavity SCC patients received surgery with curative intent, this percentage further increased over the years to nearly 80% in 2014 (Appendix 6.5, Figure 26). Over the same time span, the proportion of patients who received primary RT and the proprotion of patients for whom no treatment was recorded further decreased. For patients with oropharyngeal, hypopharyngeal or laryngeal SCC, the way they were treated changed somewhat over time, but no clear trends could be identified (Appendix 6.5, Figure 26 and Figure 27).

5 INDICATOR RESULTS

5.1 Quality of diagnosis and staging in squamous cell carcinoma of the head and neck

5.1.1 Timeliness of start of first treatment with curative intent (DS-1)

Timely treatment of (head and neck) cancer is essential, not only to increase the chance for cure and to increase the survival rates, but also to alleviate the symptoms as soon as possible.

National results

Overall, **the median interval from diagnosis to first treatment with curative intent was 32 days**; while 25% of all patients were treated within 19 days after they were diagnosed with an HNSCC, a quarter of patients were waiting 46 days or longer to start treatment (Appendix 7.1.1, Table 92). No big differences were observed between anatomic sites, except for oral cavity SCC patients for whom 50% of the patients received their first treatment 27 days after their diagnosis, which may in part be explained by the fact that 73.4% of these patients received a surgical intervention with curative intent, while for the other anatomic sites, the primary treatment was radiotherapy (for 62.8% of oropharyngeal cancers, 69.9% of hypopharyngeal cancers and for 62.0% of laryngeal cancers).

When treatment includes **surgery, either as first treatment or following a neoadjuvant treatment** (radiotherapy with or without systemic therapy), the time delays were shorter (**24 and 26 days respectively**); 75% of these patients started their treatment with a delay of 35 (surgery following a neoadjuvant treatment) or 39.5 (surgery as first treatment) days or longer after their diagnosis. Because patients with stage I HNSCC were more often treated with surgery compared with their peers with higher stage SCC, the median time to start treatment was shorter for the former group (median interval of 28 days).

The median delay to start **primary radiotherapy was 36 days**. The observation that the time delay is longer for radiotherapy than for surgery, may (among others) be explained by the fact that for radiotherapy the preparatory phase needs more time. In addition, patients who will receive radiotherapy in the head and neck region, should have a thorough pre-radiotherapy dental assessment and, when indicated, treatment. In case dental extractions are performed, it is important to allow sufficient healing time prior to the commencement of radiotherapy.

Patients who received their first treatment in the same centre where the diagnosis was confirmed, were treated within a shorter time frame than patients who were referred to another centre for treatment (median interval: 26 vs. 37 days). The same observation was reported in the Netherlands, where a better survival was nevertheless obtained in patients who were referred to a Head and Neck Oncology Centre (HNOC).

The median interval from diagnosis to treatment start at the five Danish HNOC was one week shorter (i.e. 25 days in 2010) than what was observed in our study (Appendix 7.1.1, Table 93 and Table 94); the most pronounced reduction was seen in waiting time for definitive radiotherapy which decreased from 40 to 19 days between 2002 and 2010.[86] Yet, the Belgian results compared favourably with those reported in other European countries such as UK (2013-2014)[87], France (2008-2010)[88] and the Netherlands (2005-2011)[89] (see also Appendix 7.1.1 for more details).

Comparison between centres

A large dispersion was observed between centres; the median time from incidence to treatment varied between 0 and 50 days when benchmarking was done based on the centre of main treatment (Figure 4) and from 0 to 66 days when benchmarking on the centre of diagnosis (Appendix 7.1.1, Figure 28).

Figure 4 – Time from incidence date to first treatment with curative intent, by centre of main treatment (2009-2014)
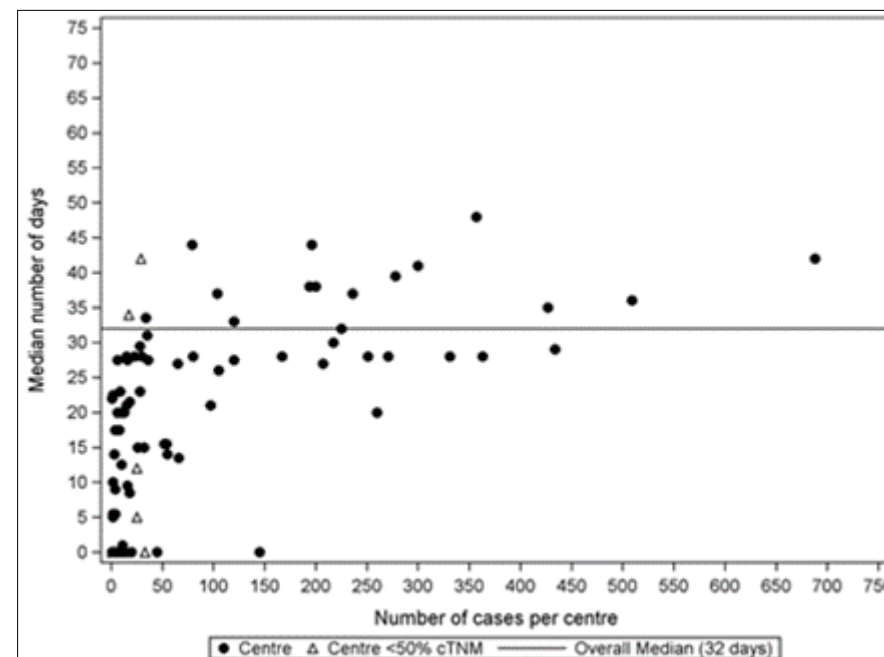
Note: 96 centres reported in the scatter plot; centres which reported for less than 50% of their assigned patients cTNM to the BCR, are represented by an open triangle.
Source: BCR – IMA

Key Points

- **Median waiting time between diagnostic confirmation and start of treatment for patients with a HNSCC in Belgium was 32 days (IQR: 19-46 days);**

- **Oral cavity SCC patients were treated more rapidly after their diagnostic confirmation than other HNSCC patients (median 27 days; IQR: 8-42);**

- **When first treatment is surgery, the median time interval was shorter compared to primary radiotherapy (24 days versus 36 days);**

- **Patients who received their first treatment in the same centre where the diagnosis was confirmed were treated within a shorter time frame than patients who were referred to another centre (median interval: 26 vs. 37 days). The same observation was reported in the Netherlands, where a better survival was nevertheless obtained in patients who were referred to a Head and Neck Oncology Center (HNOC).**

5.1.2 MRI and/or contrast-enhanced CT of the primary site and draining lymph nodes before treatment (DS-2)

Appropriate imaging helps to improve the accuracy in defining the extent of disease and thus informs the MDT in the treatment planning process.[87] According to the Belgian guidelines, MRI is the preferred technique for primary T- and N-staging in oral cavity SCC and highly recommended in hypopharyngeal, laryngeal and oropharyngeal SCC. However, for all anatomic sites, a contrast-enhanced CT can also replace MRI when (a good) MRI is technically impossible, likely to be distorted, or not timely available.[22, 23]

The importance of the staging before starting a treatment is well recognized. Our expert group considered that the target to be reached would be 90%, which is in line with the target set by the British Association of Head & Neck Oncologists (BAHNO, 90%)[87] while in Scotland this target was set at 95%.[34] The tolerance within this target is designed to account for the fact that some

patients may have significant comorbidities or may not be fit for investigation and/or treatment.

National results

Yet, our data showed that the proportion of **HNSCC patients who received treatment with curative intent in whom an MRI and/or CT was obtained within six weeks before the start of the first treatment, was 82.5%**, which is below the target set by the clinical experts. In patients with oral cavity SCC, this proportion was even lower (74.9%), while the objective was almost reached in the group with oropharyngeal (89.3%) and hypopharyngeal SCC (89.5%) (Appendix 7.1.2, Table 95). Females (χ^2 29.01; p<0.001), patients>80 years (χ^2 38.13; p<0.001) and patients presenting with a clinical stage I (χ^2 173.72; p<0.001) received less frequently a staging by MRI and/or CT than their counterparts (Appendix 7.1.2, Table 95 and Table 96). There is also a large difference between patients who were primarily treated with radiotherapy (92% with MRI/CT) and patients treated with surgery, with or without radiotherapy (70.5%) (Appendix 7.1.2, Table 95). According to the experts, a diagnostic excision biopsy may be performed without prior CT or MRI in small tumours. That may explain why the rate of pre-operative imaging is lower in surgically treated patients. Also, it must be acknowledged that some CTs identified in the database may have been performed for RT treatment planning.

Although MRI is preferred over CT, CT was used 2.2 times more frequently than MRI (Appendix 7.1.2, Table 97). The likelihood to obtain a CT rather than a MRI is higher for all anatomic sites, but particularly for hypopharyngeal cancer (three times higher) and laryngeal cancer (four times higher). The difference is also striking in older patients. The observation that in patients with laryngeal and hypopharyngeal SCC, CT is more used than MRI, may (in part) be explained by the fact that the longer duration of an examination with MRI in these patients causes difficulty with breathing and may often be associated with movement artefacts. Moreover, performing an MRI of the larynx and hypopharynx requires an experienced radiologist coupled with adapted high end hard (MR and coils) and software (right sequences and software to speed-up examination).

Moreover, since the number of CT scans registered on 1 January 2018 was at least two times higher than the number of MRI scans (Appendix 7.1.2), we can suppose that a similar ratio was also relevant for the period 2009-2014. This higher availability of CT scans can largely explain the more frequent use of this equipment compared to MRI for the staging of HNSCC patients.

As is presented in Table 98 (Appendix 7.1.2), only 10.1% of patients who did not have a MRI or CT, received a PET(/CT) within six weeks before start of the first treatment. This proportion is likely to increase in the near future as nowadays more and more hospitals can do PET(/CT) with high quality CT.

Taking all information into account, 15.7% of HNSCC patients who received treatment with curative intent did not receive a staging using MRI, CT or PET(/CT) in Belgium (2009-2014). This proportion is however slightly lower than the proportions reported either in England and Wales (2013-2014),[87] or in Ontario (2010)[90] where 17.8% and 28% respectively of all diagnosed patients did not obtain staging information with PET(/CT), CT, MRI or ultrasound prior to treatment (Appendix 7.1.2, Table 100). The reported results were not split in subgroups according to anatomic sites and treatment strategies which makes full comparison with the Belgian data impossible.

Comparison between centres

Almost one third of the centres fell above or below the 99% prediction interval. The lowest scores were observed for hospitals with lower number of cases, but also some hospitals with 150 to 300 patients score below the prediction interval (Figure 5). Some of the centres displayed very low proportions (≤ 60%). Only fifteen centres reached the target (≥ 90%) for their patients.

Figure 5 – Proportion of HNSCC patients who received treatment with curative intent in whom an MRI and/or CT was obtained within six weeks before the start of the first treatment, by centre of main treatment (2009-2014)
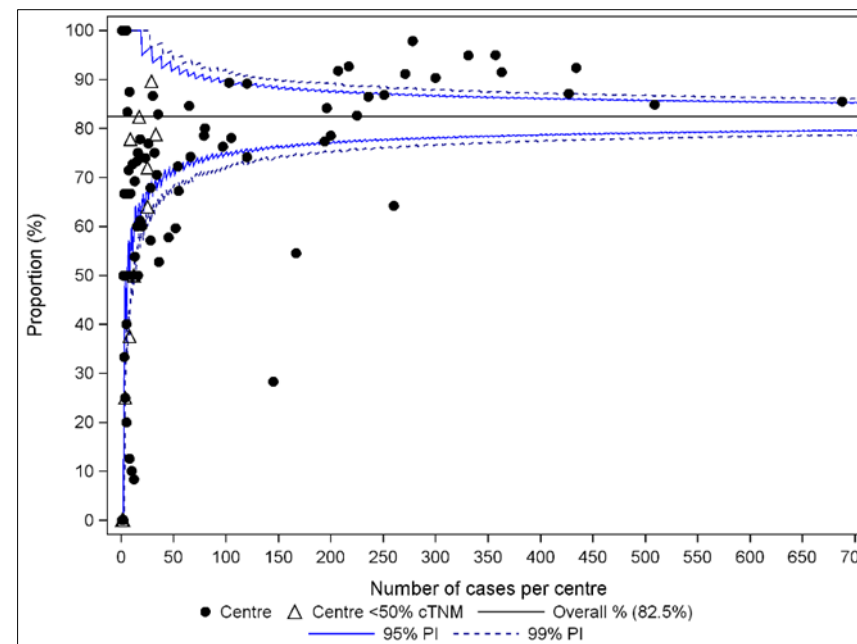
Note: 96 centres reported in the funnel plot; centres which reported for less than 50% of their assigned patients cTNM to the BCR, are represented by an open triangle.
Source: BCR – IMA

Key Points

- **The proportion of HNSCC patients who were staged with MRI and/or CT before the start of the first treatment, was 82.5%, which is below the adopted target (≥ 90%);**

- **The lowest scores were observed for hospitals with lower number of cases, but also some hospitals with 150 to 300 patients score below the prediction interval;**

- **Although MRI is the preferred technique in oral cavity SCC and is highly recommended in hypopharyngeal, laryngeal and oropharyngeal SCC, a CT was more frequently performed than an MRI, irrespective of the anatomic site;**

- **Overall, 15.7% of HNSCC patients who received treatment with curative intent did not receive an adequate staging using MRI, CT or PET(/CT).**

5.1.3   T, N and M staging in new cases of SCC of the head and neck (DS-3)

As stated before, accurate staging is an essential step in the clinical cancer pathway. To capture this information, a proxy approach was used by evaluating the completeness of the data transferred to the BCR, since it was impossible to check the medical files of all HNSCC patients. Moreover, in Belgium, hospitals have to transfer all new cancer diagnoses, irrespective of the fact that the patient is discussed during a multidisciplinary team meeting (MDT), to BCR.[91] In addition, the pathology laboratories encode the received specimens following classification rules approved by the Consilium Pathological Belgicum and transfer the information yearly to the BCR, as stated in the law.[92]

For a good understanding of the data it is important to mention that also stages reported as TxNxMx are counted as 'not reported'.

National results

a)   Clinical stage

Our data showed that the proportion of patients with HNSCC who have their **cTNM stage** reported to the BCR was **80.5%**, which is below the target defined by the experts (95%). This proportion was higher among patients with hypopharynx (89.0%) and oropharynx (85.3%) SCC and among those receiving palliative RT (100%), primary (Systemic)/radiotherapy (without major surgery; 88.8%) and primary systemic therapy (no major surgery, no radiotherapy; 86.4%) (Appendix 7.1.3, Table 101). According to the experts, part of the lower than expected proportion of reporting on cTNM can possibly be found in the underreporting of Tis and T1, especially in case of laser resections and excisional biopsies of the oral cavity. But also, cTNM may not be reported to BCR in those cases where no malignancy was suspected before the surgical intervention.

As was mentioned earlier (see section 4.2), a MDT was recorded for 82.3% of the total study population. The proportion of HNSCC patients who have their cTNM reported to the BCR was much higher among those who were discussed during a MDT (87.3% vs. 49.0%), and this was the case for all anatomic sites (Appendix 7.1.3, Table 102).

Among the 667 patients who received no treatment, only 66.1% had a cTNM stage reported, probably because the general state of these patients did not allow any physical examination, imaging, endoscopy, biopsy or surgical exploration to obtain the necessary information.

Since the data reporting and collection vary across countries, caution is needed in the comparison of our results with data from other countries. In England and Wales, the recording of pre-treatment staging only reached 86.8% in 2013-2014, which points out the difficulties in accurate pre-operative staging despite sophisticated imaging (Appendix 7.1.3, Table 106).[87] Although variation between and within English cancer networks was lower than the previous year, nine networks attained over 85%, whereas four networks achieved less than 80%. Finally, compared to other anatomic sites, oral cavity SCC had the highest proportion of unknown pre-treatment staging (16.3%), which is similar to what we observed in Belgium.

b) Pathological stage

The post-surgical histopathological classification (pTNM) is based on the evidence acquired before treatment, supplemented or modified by the additional evidence obtained from surgery and from pathological examination. This is both important to accurately define actual stage as well as indicating the need for adjuvant treatment.

In our data, the proportion of patients with HNSCC who had surgery, who have their **pTNM stage** reported to the BCR was **78.4%**, which is again below the target of 95% (Appendix 7.1.3, Table 103). The pTNM reporting was slightly higher for patients with SCC of the oral cavity (82.7%) and hypopharynx (80.5%). The proportion of HNSCC patients who have their pTNM reported to the BCR was again sharply higher among those who were discussed during a MDT (81.7% vs. 64.5%), and this was the case for all anatomic sites (Appendix 7.1.3, Table 105). Discussion at an MDT and adequate reporting of pTNM by the pathologists are highly recommended to improve adequate staging of surgically treated tumours. Finally, in England and Wales, post-surgical histopathological staging was only reported for 81.6% of HNSCC, with some variation between cancer networks (Appendix 7.1.3, Table 106).[87] However, caution is needed in comparing these results since the data reporting and collection vary across countries.

Comparison between centres

About 30% of the centres were situated outside the funnel 99% PI for clinical staging (Figure 6) and about 20% for pathological staging (Figure 7). Centres with a score above the upper funnel limit are in comparison with other centres well performing centres, yet as can be deduced from both plots not all centres above the 99% prediction interval reach the target set at 95%.

Figure 6 – Proportion of patients with HNSCC who have their cTNM reported to the BCR, by centre of first treatment (2009-2014)
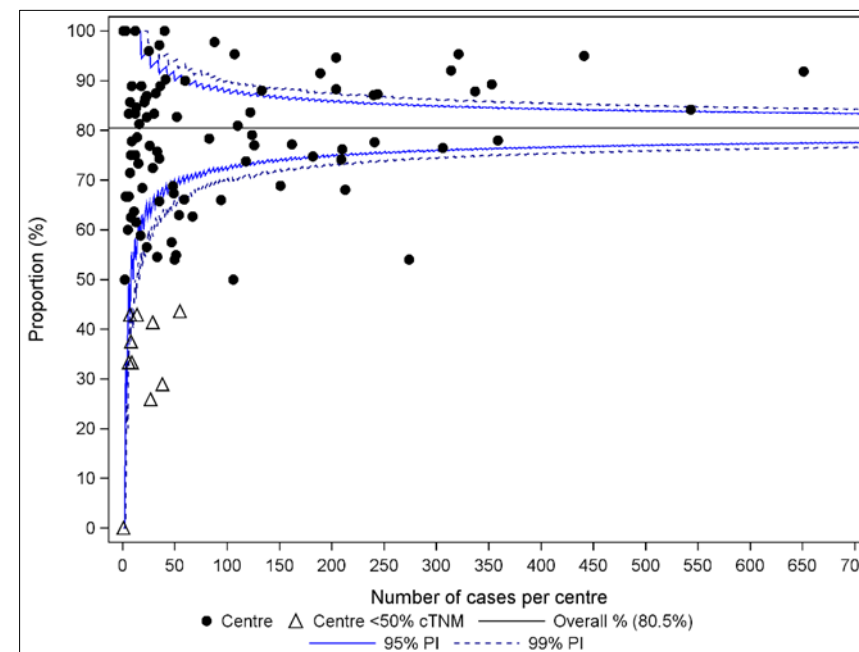
Note: 101 centres reported in the funnel plot; 132 patients were not included in the analyses because they could not be assigned to a first treatment centre, but their data are included in the analyses for the overall result; centres which reported for less than 50% of their assigned patients cTNM to the BCR, are represented by an open triangle.
Source: BCR – IMA

Figure 7 – Proportion of patients with HNSCC who had surgery with curative intent, who have their pTNM reported to the BCR, by centre of main treatment (2009-2014)
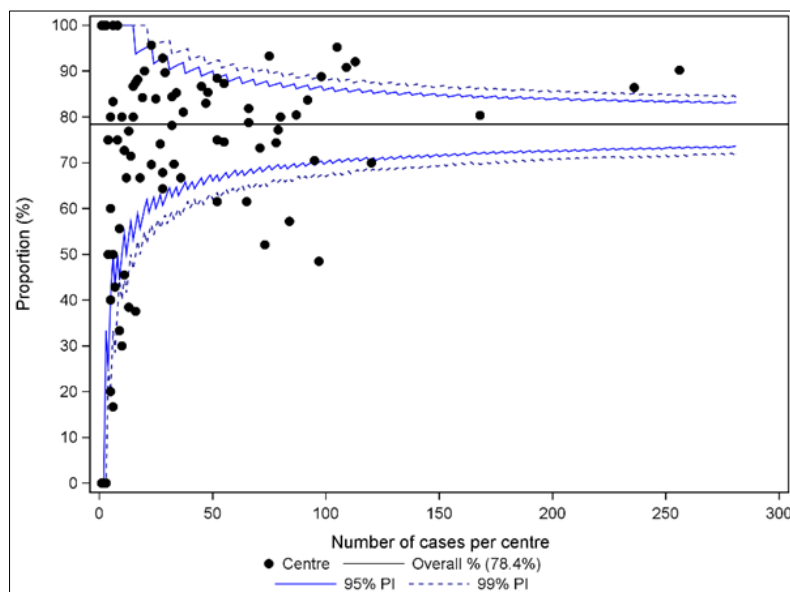
Note: 96 centres reported in the funnel plot
Source: BCR – IMA

Key Points

- **The proportion of patients with HNSCC who had their cTNM stage reported to the BCR was 80.5%;**

- **The proportion of patients with HNSCC who had their pTNM stage reported to the BCR after surgery was 78.4%;**

- **As these proportions are far below the target to be reached (95%), focused effort is required to adequately report pre-treatment and post-surgical histopathological stages.**

5.1.4 *FDG-PET(/CT) before treatment (DS-4)*

According to the KCE guidelines, a whole-body FDG-PET(/CT) is not recommended for the evaluation of metastatic spread and/or the detection of second primary tumours in patients with stage I-II HNSCC, while it is recommended for patients with stage III-IV HNSCC.[22, 23]

National results

After discussion with the experts, it has been decided that the use of FDG-PET(/CT) in **stage I-II HNSCC patients** should be less than 5%. Yet, our data showed that the proportion of stage I-II HNSCC patients who underwent any treatment and in whom a whole-body FDG-PET(/CT) was performed, was 22.9%, which is largely above the target and thus unnecessary. Moreover, the proportion was higher among patients with oropharynx (36.0%) and hypopharynx (37.9%) SCC, among females (26.4%), and decreased slightly across age groups (from 25.1% for age < 50 years to 15.9% for age ≥ 80 years) (Appendix 7.1.4, Table 107). This proportion was also higher in stage II (31.5%) patients.

On the other hand, in **stage III-IV HNSCC patients** FDG-PET(/CT) is recommended and hence a target of ≥ 90% was suggested by the experts. However, our data showed that the proportion of stage III-IV HNSCC patients who underwent non-palliative treatment in whom a whole-body FDG-PET(/CT) was performed, was 47.6%, which is far below the target. Again, there was some variation across subgroups: the proportion was higher among patients with oropharynx (53.2%) and hypopharynx (53.7%) cancer, with stage IVA/B (49.1%) and IVC (56.1%), and among those receiving primary (Systemic)radiotherapy (no major surgery) (50.9%) and primary systemic therapy (no major surgery, no RT) (54.1%), while it was lower among patients aged 80+ years (29.8%) (Appendix 7.1.4, Table 108).

So, globally, in Belgium, 39.2% of HNSCC patients (with known clinical stage) underwent FDG-PET(/CT) within six weeks before start of the first treatment. In comparison, in England and Wales, 10.6% of patients were recorded as having undergone FDG-PET(/CT) prior to treatment (November 2013 - October 2014, Appendix 7.1.4, Table 109).[87] However, the reported results were not split in subgroups according to cancer stage, which makes

full comparison with the Belgian data impossible. In England and Wales, the most frequent anatomic site where FDG-PET(/CT) was carried out was the pharynx, with 23.0% for nasopharynx, 19.3% for oropharynx, and 15.5% for hypopharynx, which is similar to what we observed in Belgium. Comparing our data with other countries than the UK was not possible, since, to our knowledge, the use of PET(/CT) in patients with HNSCC has not been reported for other representative patient groups.

Comparison between centres

For both indicators, more than 20% of the centres were falling outside the 99% prediction interval (Figure 8 and Figure 9). Only 44 out of 86 centres reached the target (≤ 5%) set for FDG-PET(/CT) in stage I-II HNSCC patients (scores between 0 and 100%) and for FDG-PET(/CT) in stage III-IV HNSCC patients, no centre reached the target (≥ 90%) (scores between 0 and 84%). According to the experts, several factors may explain this variability. First of all, the overall availability of and access to FDG-PET(/CT) was far from optimal during the study period (2009-2014). Part of the variability may also be explained by the reimbursement rules at the time of the study. Until 2016 the list of recognized indications for PET-reimbursement was limited, e.g. primary head and neck cancer staging was not in the indication list. [g] Last but not least, it must be mentioned that overall there may be a slight underestimation of the real number of patients who underwent FDG-PET(/CT), as imaging performed in the frame of clinical studies (e.g. imaging studies) is not included in the database (as they cannot be billed). Also, in some patients a FDG-PET(/CT) may have been performed in the referring centre and may have fallen outside the time frame of six weeks set for this quality indicator.

Figure 8 – Proportion of clinical stage I-II HNSCC patients who underwent any treatment in whom a whole-body FDG-PET(/CT) was obtained within six weeks before start of the first treatment, by main treatment centre (2009-2014)
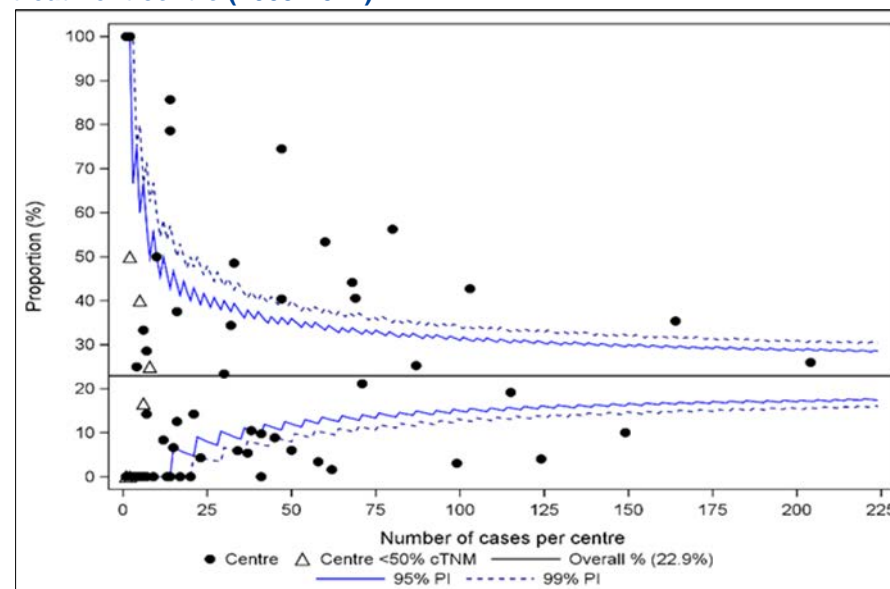
Note: 86 centres reported in the funnel plot; one patient is not included in the analyses as he/she could not be assigned to a treatment centre, but his/her data are included in the analyses for the overall result; centres which reported for less than 50% of their assigned patients cTNM to the BCR, are represented by an open triangle.
Source: BCR – IMA

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[g]   There was however a possibility to bill for non-recognized indications (including primary head and neck) using a different nomenclature code (at a lower fee) but not all centres were happy to do so.

Figure 9 – Proportion of clinical stage III-IV HNSCC patients who underwent non-palliative treatment in whom a whole-body FDG-PET(/CT) was obtained within six weeks before start of the first treatment, by main treatment centre (2009-2014)
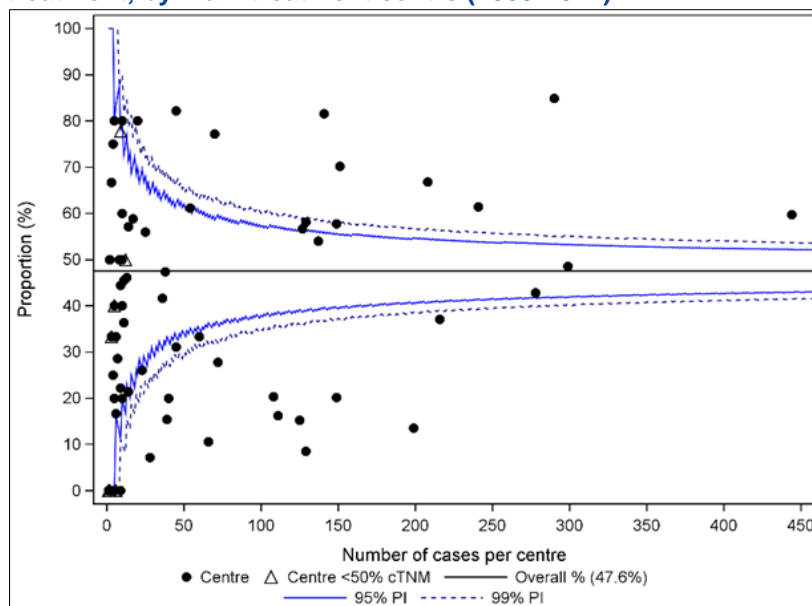
Note: 87 centres reported in the funnel plot; centres which reported for less than 50% of their assigned patients cTNM to the BCR, are represented by an open triangle
Source: BCR – IMA

Key Points

- **The use of FDG-PET(/CT) was at 23% in clinical stage I to II HNSSC patients. This proportion is far above the target to be reached (≤ 5%);**
- **The use of FDG-PET(/CT) was at 48% in clinical stage III to IV HNSCC patients. This proportion is far below the target to be reached (≥ 90%).**

5.2 Quality of treatment in squamous cell carcinoma of the head and neck

5.2.1 Single modality treatment in stage I-II (T-1)

National results

Overall, 78.1% of patients with early stage HNSCC who received treatment with curative intent, received a single modality treatment (Appendix 7.2.1, Table 110). This proportion is slightly lower than the target set by the clinical experts (i.e. 80-85%). Yet, important differences are observed among the different anatomic sites: 90% of patients with early stage laryngeal SCC were offered a single modality approach while the respective proportion for their peers with hypopharyngeal SCC was only 59.6%. This could be explained by the fact that even for cT1 N0 hypopharyngeal SCC, the probability of occult nodal metastases is around 40 to 60% and hence all these patients, exception made for pN1 patients, should receive adjuvant RT. On the contrary, in cT1-2 true glottic SCC postoperative radiotherapy is rarely indicated as these patients are often free from occult metastases.

Among the early stage HNSCC patients who had surgery, 80.4% of the patients with a pathological stage I-II were treated with surgery only, while this proportion dropped to nearly half (41.1%) in patients with a pathological stage III. One can also observe that the proportion of patients being treated with either surgery alone or radiotherapy alone is increasing with increasing age.

Suboptimal staging before treatment and subsequent stage migration (especially for oral cavity SCC), and incomplete resection may explain why a number of patients needed postoperative radiotherapy. Furthermore, the age depending variation may be explained by both maximisation of treatment i.e. more aggressive treatment in younger patients and de-escalation of treatment in older age groups, due to comorbidities or frail general condition. Multidisciplinary team meetings (MDT) both before and after surgery are recommended in order to minimize the need for multimodality treatment. Also, there may be a trend in younger patients with a HNSCC that is amenable both for (endoscopic) surgery and radiotherapy,

to choose surgery as a first option in order to 'save the radiotherapy' in case recurrences and/or second primaries (which are often not amenable for surgery anymore) are detected. Furthermore, some of the older patients may have contra-indications for long general anaesthesia, prohibiting some surgical procedures.

Among the 2 131 patients who did not receive any systemic treatment, 252 (11.8%) received surgery followed by RT and only a small number of patients received RT followed by surgery (N=15) or RT in combination with LND (N=19) (Appendix 7.2.1, Table 111). From Table 111 we can also observe that among cstage I patients comparable proportions are treated with surgery only (47.5%) or RT only (44.3%), while in cstage II, a higher proportion is treated with RT only (50.2%), compared to surgery only (28.6%). In the cstage II group, 19.4% of patients received RT after surgery.

Overall 231 patients were treated with systemic therapy in combination with surgery and/or radiotherapy: 138 (59.7%) received systemic therapy in combination with radiotherapy and another 72 (31.2%) received surgery followed by systemic therapy in combination with radiotherapy (Appendix 7.2.1, Table 112). Among the 286 patients who were treated with a combination of surgery and radiotherapy, the majority (88.1%) received surgery followed by radiotherapy (Appendix 7.2.1, Table 113).

The comparison of these data with international data is somewhat cumbersome: only few international reports (presenting data from more than one institution) were available (see Appendix 7.2.1, Table 114). In addition, the comparison should be done with caution since the denominator applied in the present study (i.e. patients with clinical stage I or II disease who received treatment with curative intent (surgery or radiotherapy or the combination of both) with or without chemotherapy/targeted therapy) was stricter than what could be deduced from the international publications (i.e. the total sample of patients with early stage SCC).[93-95] Even then, it is fair to say that a single modality treatment was more frequently offered to early stage hypopharyngeal SCC patients in the Netherlands than in Belgium (83.9% vs. 59.6%), while the opposite was observed for laryngeal cancer (at least 37% in the US vs. 90.0% in Belgium).[93, 95] With respect to early stage oral cavity SCC, the Belgian data were comparable to those reported for Ireland (69.9% vs. 76.3%).

Comparison between centres

As can be observed in Figure 10, almost all centres fell between the 99% prediction intervals of the funnel plot; however, it is important to mention that 40 of the 86 centres treated less than ten patients (who received surgery and/or radiotherapy with curative intent) over the six year study period.

Figure 10 – Proportion of patients with early stage (cI or cII) HNSCC who were treated with a single-modality approach, by centre of main treatment (2009-2014)
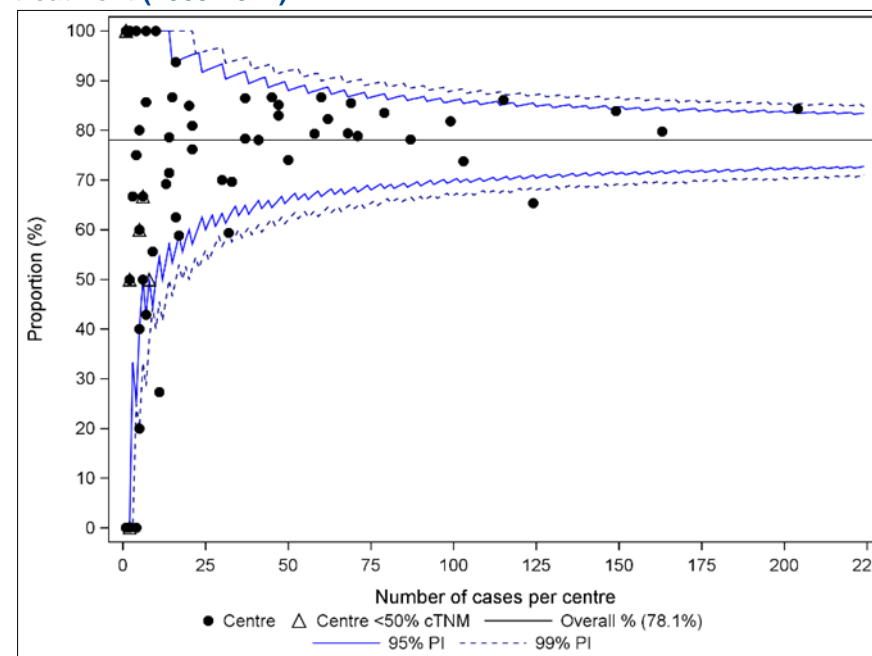
Note: 86 centres reported in the funnel plot; centres which reported for less than 50% of their assigned patients cTNM to the BCR, are represented by an open triangle.
Source: BCR – IMA

Key Points

- **A single modality approach was offered to 78.1% of patients with early stage HNSCC, which is close to the target set by the clinical experts (i.e. 80-85%);**

- **Considerable differences were observed among the different anatomic sites (between 59.6% and 90.0%) and the different age groups (between 69.7% and 89.9%).**

5.2.2 Total laryngectomy in T4a laryngeal cancer (SX-1)

According to the KCE guideline, total laryngectomy should be considered in patients with T4a laryngeal cancer.[23]

National results

In our database, only 116 patients were identified with non-metastatic T4a laryngeal cancer; 73 of them (62.9%) underwent a total laryngectomy (Appendix 7.2.2, Table 115). This proportion is below the target defined by the experts (i.e. ≥80%).

In the present analysis 212 patients were excluded since their TNM staging information was not specific enough, i.e. only T4 was reported to BCR, without any further specification whether it was T4a or T4b. It is evident that extra efforts are needed to improve the quality of data reported to BCR.

While the proportion of patients with non-metastatic T4a laryngeal cancer who underwent total laryngectomy in Belgium is slightly lower than in Maryland in 2000-2009 (69% for all laryngeal cancer cases)[96], it is similar to the results from Korea (59.6% for T4a laryngeal cancer cases with thyroid cartilage invasion).[97] Interestingly, the proportion in Belgium is considerably higher than in the Netherlands (30.9% for T3-T4 laryngeal cancer cases; Appendix 7.2.2, Table 116).[98] This might be due to the fact that the Dutch guidelines for treating laryngeal cancer changed in 1999 after the publication of a consensus document by the Dutch Cooperative Head and Neck Oncology Group.[99] Since then, patients with T3 laryngeal cancer were

preferably irradiated, while patients with T4 laryngeal cancer underwent in most centres a laryngectomy and adjuvant RT. However, caution is needed in comparing our results with international data, because our study is limited to T4a laryngeal SCC cases and the sample is very small.

Also in Belgium, treatment protocols for T4a laryngeal cancer have changed over the years, with total laryngectomy being the recommended treatment only in recent years. An increase in the proportion of T4a laryngeal cancer treated with total laryngectomy is expected in the future.

Comparison between centres

The sample was too small for a correct assessment of the variability between centres. Due to the low sample size (only three centres with at least ten patients), the prediction intervals in Figure 11 are very wide; the results should be interpreted with caution.

Figure 11 – Proportion of patients with non-metastatic T4a laryngeal cancer who underwent total laryngectomy, by main treatment centre (2009-2014)
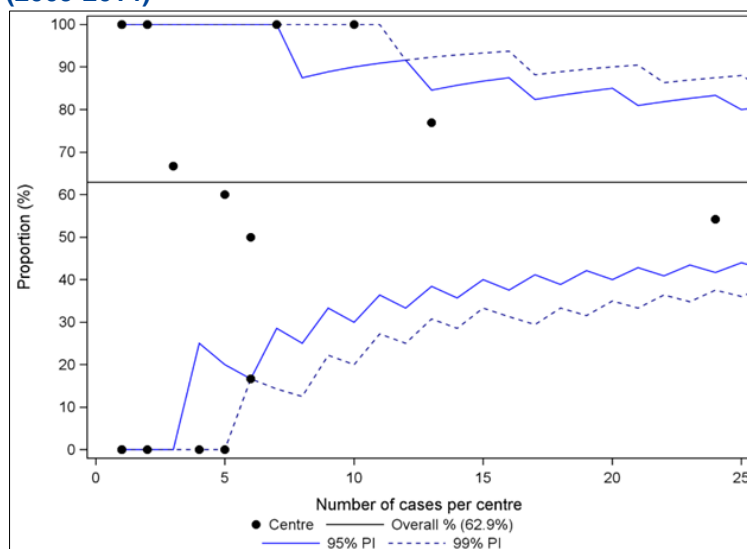
Note: 33 centres reported in the funnel plot
Source: BCR – IMA

Key Points

- **The proportion of patients with non-metastatic T4a laryngeal cancer who underwent total laryngectomy was 62.9%, which is below the target (≥80%);**

- **Many patients could not be included in this analysis since their TNM staging information reported to BCR was not specific enough.**

5.2.3 Timeliness postoperative radiotherapy (RT-1)

According to the KCE guideline postoperative radiotherapy should be started within 6 weeks after surgery and completed within 11-13 weeks after surgery, which is in line with other guidelines.[23,87,100] While other guidelines and audit reports (cf. infra) concentrated on the start of postoperative radiotherapy within six weeks after surgery, it was opted to focus here on the fact that radiotherapy was completed within thirteen weeks after surgery, as the experts indicated that the total treatment time is the most important aspect. Therefore, when post-operative RT (PORT) cannot be started within six weeks (e.g. in case of post-operative complications), this can be compensated during the RT course so that all fractions are given within thirteen weeks after surgery.

National results

While the clinical experts suggested that ≥ 90% of patients should have completed PORT within thirteen weeks after surgery, only 48.5% of patients ended their PORT (whether or not completed) within this time frame (Appendix 7.2.3, Table 117). The target was not reached within a more liberal time frame of fifteen weeks either, as only 71.7% of patients ended their PORT by that time (Appendix 7.2.3, Table 118). The highest percentage of patients having ended their PORT within thirteen weeks after surgery was obtained in patients with oropharyngeal cancer (58.6%; median 89 days (12.7 weeks); Q1-Q3: 79-102) while the lowest percentage was reported in patients with a cancer of the oral cavity (45.1%; median 93 days (13.3 weeks); Q1-Q3: 85-112) (Appendix 7.2.3, Table 118 and Table 119). Patients who were referred for RT to another centre, had a lower chance of having their RT ended within thirteen weeks after surgery (44.3% vs. 51.9%; Appendix 7.2.3, Table 117).

In the UK, the last audit on 2014 data also reported disappointing results: only two cancer networks achieved a median interval less than 42 days (i.e. 6 weeks) and the variability in the time to start PORT between cancer networks was large (from a median of 39 days (5.5 weeks) to a median of 76 days (11 weeks)).[87] In the US, the analysis of the National Cancer Database (2006-2014) also revealed substandard results, since only 44.3% of patients started PORT within 6 weeks of surgery, and this percentage

decreased over time (47.1% of patients in 2006 vs. 41.3% of patients in 2014; p<0.001). Fragmentation of care over different facilities, long hospital stay after surgery, unplanned hospital readmission within 30-days of surgery, use of IMRT or proton therapy were correlated with delayed initiation of PORT.[100]

Comparison between centres

Hospitals varied considerably with regard to the proportion of patients in whom postoperative radiotherapy was ended within 13 weeks after surgery. For three hospitals the results were worse than what can be expected based on random variability, and for another three hospitals results were better. Deviating results are observed for hospitals with a lower number of patients as well as for those with a higher number of patients. This dispersion was observed when benchmarking was performed based on the centre of main treatment (Figure 12) as well as on the centre of radiotherapy (Figure 13). It is also worthwhile to mention that the 1 632 patients, who had surgery with adjuvant radiotherapy, were distributed among 85 treatment centres; many of them treated less than twenty of these patients over the six year study period. The high variability between centres is also visible when benchmarking is performed based on centre type (i.e. RT versus non-RT centre, Appendix 7.2.3, Figure 29) and when the start date of post-operative RT is evaluated (Appendix 7.2.3, Figure 30, Figure 31 and Figure 32). From the scatterplots it can be deduced that the median end date of post-operative RT is nearly within the intended 11-13 weeks for all anatomic sites (i.e. 77-91 days), yet in many centres the median is far above this time frame while in some centres the median is below 77 days (Appendix 7.2.3, Figure 33 and Figure 34).

Figure 12 – Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was ended within thirteen weeks after surgery, by main treatment centre (2009-2014)
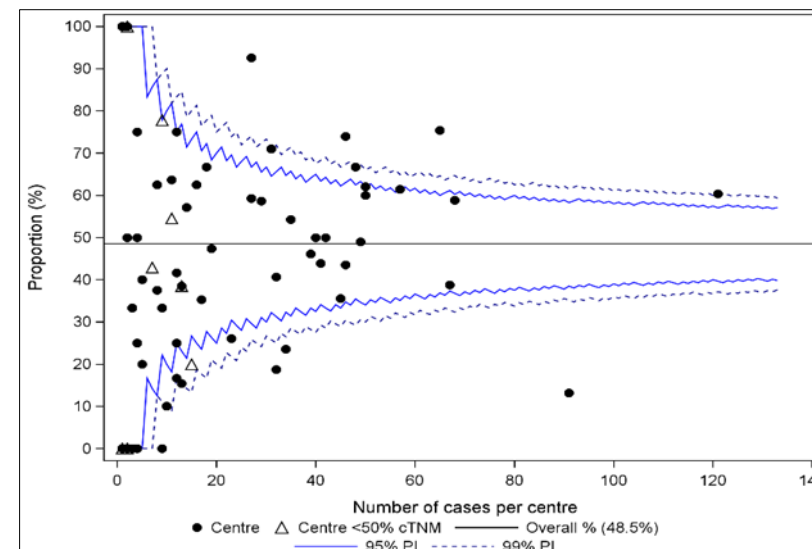
Note: 85 centres reported in the funnel plot; 10 centres which reported for less than 50% of their assigned patients cTNM to the BCR, are represented by an open triangle.
Source: BCR – IMA

Figure 13 – Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was ended within thirteen weeks after surgery, by radiotherapy centre (2009-2014)
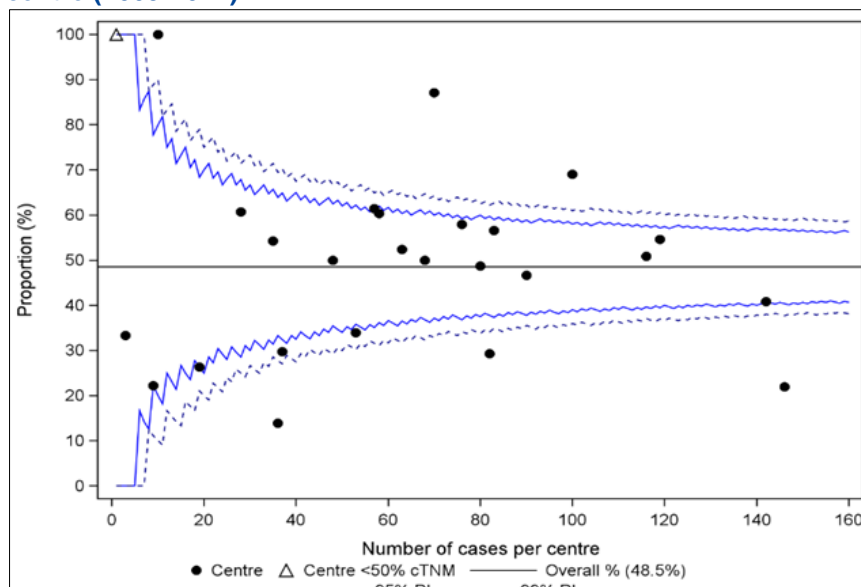
Note: 26 centres reported in the funnel plot; 1 centre which reported for less than 50% of its assigned patients cTNM to the BCR, is represented by an open triangle; 3 patients were not included in the analyses as they could not be assigned to a RT centre, but their data are included in the analyses for the overall result.
Source: BCR – IMA

Key points

- **48.5% of HNSCC patients ended their postoperative radiotherapy within thirteen weeks after surgery, which is much lower than the set target (≥ 90%); the median interval from surgery to end PORT was 92 days;**

- **The 1 632 patients who had surgery with adjuvant radiotherapy, were distributed among 85 treatment centres; many of them treated less than 20 of these patients over the six year study period;**

- **Patients who were not referred for RT had a higher chance of having their RT ended within thirteen weeks after surgery, than their peers who were referred for RT (51.9% vs. 44.3%).**

5.2.4 Primary chemoradiotherapy for locally-advanced non-metastatic disease (RT-2)

When radiation therapy is selected as primary treatment, concomitant platinum-based chemoradiation is now considered to be the standard first-line therapy to treat medically fit patients with locally-advanced HNSCC.[101]

National results

In total, 52.8% of medically fit patients (WHO performance status 0 and 1) with locally-advanced (stage III and IV) SCC of the head and neck who were treated with primary radiotherapy, received concomitant platinum-based chemotherapy (Appendix 7.2.4, Table 121). In the group of patients younger than seventy years old, this proportion was 58.2%, which is far below the target (75-80%) proposed by the experts for this age group. The lowest frequency of concomitant platinum-based CRT use is reported in patients with oral cavity SCC (42.8%) (Appendix 7.2.4, Table 121). As expected, patients who had no comorbidity were more likely to be treated with concomitant CRT (56.9%) than patients with more comorbidities (49.7% in those patients with a Charlson score 1-2 and 35.8% in those patients with a Charlson score 3-4). Concomitant CRT was also more frequently administered in patients with clinical stage IVA and IVB SCC (55%) compared to patients with clinical stage III SCC (46.4%). Yet, it must be admitted that we cannot capture in the database all contra-indications for concomitant platinum-based chemotherapy (e.g. insufficient renal function, hearing loss), so evidently the 'eligible' patients for concomitant cisplatin is overestimated. In clinical practice the denominator will be a lot smaller. So based on what we registered, we will never reach the target of 75-80%. Globally, 59.9% of patients with locally-advanced stage (stage III and IV)

non-metastatic HNSCC treated with primary RT received any concomitant systemic therapy (Appendix 7.2.4, Table 122). The majority of this group received platinum-based chemotherapy and a smaller group (7%) was treated with Cetuximab only.

It also has to be mentioned that it is very well possible that the number of patients who received induction chemotherapy has been overestimated; hence that some of these patients were treated with concomitant CRT. This problem arose from the fact that for some patients, not all fractions were correctly invoiced. The first fractions were sometimes not available in IMA – AIM data, making it difficult to clearly distinguish between induction and concomitant CRT.

Further analyses of the data revealed that 20.4% of patients with locally-advanced stage (stage III and IV) non-metastatic HNSCC received induction platinum-based chemotherapy before the start of radiotherapy (Appendix 7.2.4, Table 123), which is a potential treatment option for larynx preservation in advanced laryngeal and hypopharyngeal cancer,[102] but not in oral cavity and oropharyngeal SCC. The data presented in Appendix 7.2.4, Table 123, illustrate the non-compliance with these recommendations in practice: 29.2% and 20.5% of patients with locally-advanced stage (stage III and IV) non-metastatic oral cavity and oropharyngeal SCC treated with primary RT received induction chemotherapy, while the respective proportion was only 11.9% in laryngeal SCC.

In the UK, the annual audit 2015 reported 607 cases of advanced laryngeal cancer diagnosed and treated in 2013-2014 (Appendix 7.2.4, Table 124).[87] Of these patients, 38.9% received surgery as first active treatment, 16.5% received chemoradiotherapy as first active treatment and 12.7% underwent radiotherapy. There has been a reduction in the use of radiotherapy alone, but the use of chemoradiotherapy in advanced laryngeal cancers was unchanged from the previous annual reports.

Comparison between centres

Almost one third of the centres fell outside the 99% prediction intervals: three centres scored below and six centres above the 99% limits of the funnel plot (Figure 14).

Figure 14 – Proportion of medically fit patients with locally-advanced stage (stage III and IV) non-metastatic HNSCC treated with primary RT who received primary concomitant platinum-based chemotherapy, by main treatment centre (2009-2014)
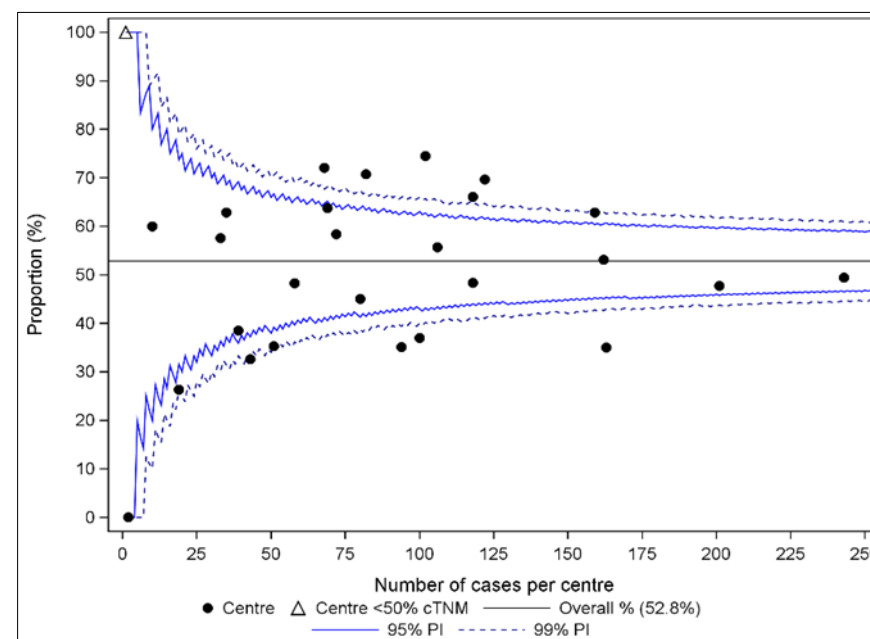
Note: 27 centres reported in the funnel plot; 1 centre which reported for less than 50% of its assigned patients cTNM to the BCR, is represented by an open triangle.
Source: BCR – IMA

Key Points

- **Concomitant platinum-based chemotherapy was offered to only 58.2% of patients younger than seventy years with locally-advanced stage (stage III and IV) non-metastatic HNSCC treated with primary radiotherapy, which may in part be explained by the fact that the number of 'eligible' patients for concomitant cisplatin is overestimated;**
- **The majority of patients who received a concomitant CRT were treated with a platinum-based regimen (i.e. cisplatinum or carboplatinum, the latter with or without 5FU).**

5.2.5 Neck imaging after primary (chemo)radiotherapy (LN-1)

According to the KCE guidelines, in node-positive HNSCC patients treated with primary (chemo)radiotherapy, a diagnostic evaluation of the neck with PET(/CT) or DW-MRI should be performed not earlier than three months after completion of primary (chemo)radiotherapy.[23]

National results

In our data, the proportion of patients with node-positive HNSCC in whom a diagnostic evaluation of the neck with PET(/CT) or (DW-)MRI was performed between ten and sixteen weeks after completion of the primary therapy (i.e. the acceptable period), was 32.7% (Appendix 7.2.5, Table 125). This proportion was higher among patients with hypopharynx (37.2%) and oropharynx (33.5%) SCC, which are indeed the two anatomic sites with the highest risk for lymph node involvement. The proportion of patients who had PET(/CT) or (DW-)MRI decreased across age groups (from 35.7% for age <50 years to 25.7% for age ≥80 years), and increased slightly with clinical stage (from 32.1% for stage III to 36.4% for stage IVC).

The results of the sensitivity analyses suggest that the proportion of patients in whom a PET(/CT) or (DW-)MRI was performed increased from 27.7% in 2009-2011 to 37.1% in 2012-2014 (Appendix 7.2.5,Table 126). It can be expected that the proportion of patients in whom a PET(/CT) or (DW-)MRI is performed, will further increase since the first randomized controlled trial showing non-inferiority of PET(/CT) -guided surveillance (compared to planned neck dissection) was only published in 2016, provided PET(/CT) availability also improves.[103]

Finally, while 41.8% of patients received a PET(/CT) or (DW-)MRI evaluation within 10-24 weeks after completion of (chemo)radiotherapy (as is recommended in the guideline), another 8.8% had a PET(/CT) or (DW-)MRI evaluation only after 24 weeks and 41.6% of patients had no image-guided =evaluation at all (Appendix 7.2.5,Table 126). Although it has been suggested that scans should be done not earlier than 10-12 weeks after completion of the primary therapy in order to have higher diagnostic accuracy, 171 patients (7.9%) underwent a scan before 10 weeks.[104, 105]

Comparison between centres

As can be observed from Figure 15, the variability among centres was high, with more than half of the centres falling outside the 99% prediction interval.

Figure 15 – Proportion of patients with node-positive HNSCC treated with primary (chemo)radiotherapy, in whom a diagnostic evaluation of the neck with PET(/CT) or (DW-)MRI was performed between ten and sixteen weeks after completion of the primary therapy, by main treatment centre (2009-2014)
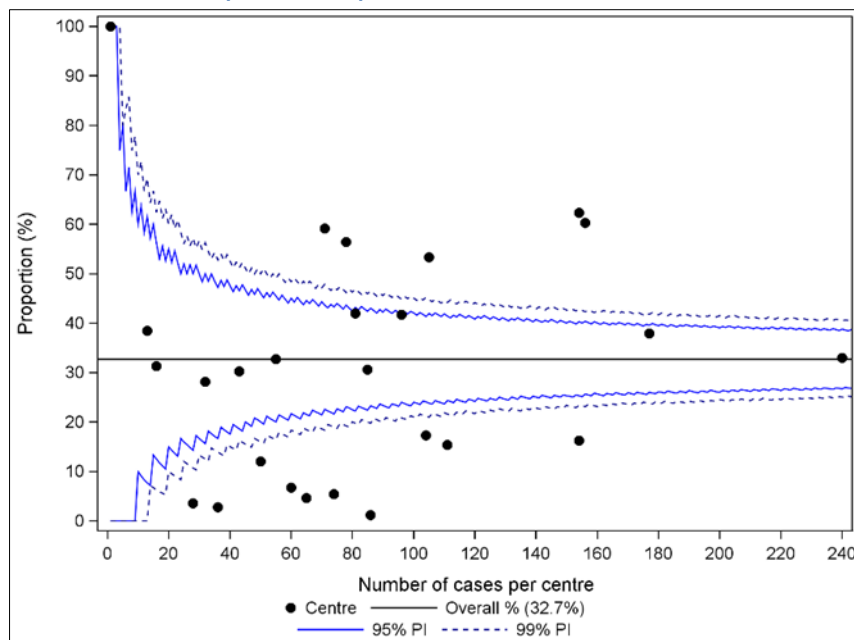
Note: 26 centres reported in the funnel plot
Source: BCR – IMA

Key Points

- **The proportion of patients with node-positive HNSCC in whom a diagnostic evaluation of the neck with PET(/CT) or (DW-)MRI was performed between ten and sixteen weeks after completion of the primary radiotherapy was 32.7%;**

- **This proportion was higher among patients with hypopharynx and oropharynx SCC, younger age groups and stage IVC;**

- **This proportion increased during the study period.**

5.2.6 Elective neck dissection in cN0M0 squamous cell carcinoma of the head and neck (LN-2)

National results

Slightly more than half of HNSCC patients (56.4%) who were staged as cN0M0/x and who had surgery with curative intent underwent an elective neck dissection (Appendix 7.2.6, Table 127). Important differences are observed among the different anatomic sites, with the highest proportion having an elective neck dissection in the subgroup with hypopharyngeal SCC (72.4%) and the lowest among patients with oropharyngeal SCC (43.3%). If the time frame was extended from two weeks up to six weeks after surgery of the primary tumour, an additional 73 patients were identified who received an elective neck dissection (Appendix 7.2.6, Table 129).

The lower than expected proportion of patients who received an elective neck dissection (target set by the clinical experts: ≥ 90%; Appendix 7.2.6, Table 127), may be explained by several factors. For example, for some T1N0 oral cavity tumours, a policy of watchful waiting may have been applied, as for tumours with a depth of infiltration below 5 mm, the risk of lymph node metastases is very low[h]. Furthermore, small glottic tumours that are categorised as T2 because of minimal invasion of the supraglottis may

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[h]   If in the revised TNM staging, tumours with an infiltration depth of more than 5 mm will be considered as T2, guidelines may no longer recommend lymphadenectomy for T1N0 tumours.

also be considered at very low risk for spread to the lymph nodes and therefore, a lymphadenectomy was omitted. Also, additional analyses revealed that 173 patients (12.8%) had adjuvant RT after surgery of the primary tumour (Appendix 7.2.6, Table 128). If after surgery on the primary tumour, an indication for RT becomes apparent, clinicians may decide to omit lymphadenectomy and treat the neck with radiotherapy as well. The rather low proportion of patients with oral cavity and oropharynx SCC for whom a LND was recorded, may be explained by the fact that in some centres sentinel lymph node biopsy (without lymphadenectomy if no metastasis in the sentinel node) is performed. These patients may have been missed in the present analyses as no billing code for sentinel node biopsy is available.

The higher the clinical stage, the higher the proportion of patients who had an elective neck dissection. This was observed in all anatomic sites (yet as the breakdown in stages per anatomic site yields many cells with small numbers, the interpretation should be done with caution, Appendix 7.2.6, Table 130).

An elective neck dissection was also less frequently performed in women (45.4% vs. 61.5%) and in older age groups (48.3% in 70-79 year-olds and 34.3% in the oldest age group). Remarkably, an elective neck dissection was more frequently performed in the subgroups with a higher Adapted Charlson Comorbidity Index (CCI 1-2: 68% and CCI 3-4: 75% vs. CCI 0: 50.6%).

The possibility to compare our data with international data is limited: an American study confined to cN0 patients with SCC of the oral cavity, based on the Surveillance, Epidemiology, and End Results (SEER) database, reported a neck dissection rate of 63.9%, which is higher than in the Belgian population (see Appendix 7.2.6, Table 132).[106] In England and Wales, 41% of patients with T1-T2 N0 tongue tumours treated by lesion excision of the tongue or partial glossectomy, underwent a neck dissection.[87]

Comparison between centres

The number of hospitals that fell outside the 99% prediction intervals was limited, and almost all of them did better than would have been expected (Figure 16). Four (rather) low-volume centres performed an elective neck dissection in all assigned patients.

Figure 16 – Proportion of surgically treated HNSCC patients with cN0M0/x with any T stage (except T1 glottic cancer), who underwent elective neck dissection, by centre of main treatment (2009-2014)
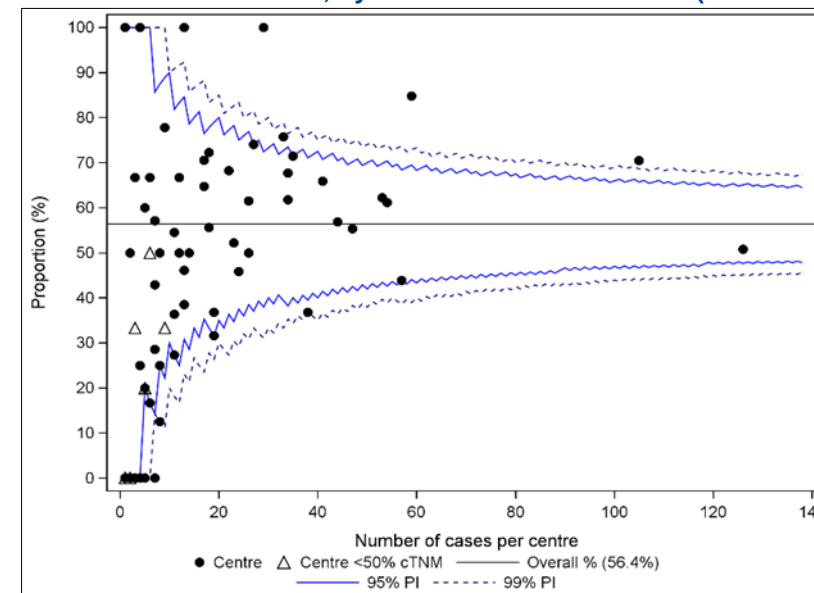
Note: 84 centres reported in the funnel plot; centres which reported for less than 50% of their assigned patients cTNM to the BCR, are represented by an open triangle; patients with clinical stage X are included in the analysis, e.g. cTxN0M0 is staged as cX.
Source: BCR – IMA

Key Points

• **Only 56.4% of HNSCC patients who were staged as cN0M0/x and who had surgery with curative intent underwent an elective neck dissection, which is much lower than the target set at ≥ 90%;**

• **30.7% of HNSCC patients who were staged as cN0M0/x and who had surgery with curative intent, did not receive any neck treatment;**

• **The higher the clinical stage, the higher the proportion of patients who had an elective neck dissection;**

• **Considerable differences were observed among the different anatomic sites (between 43.3% and 72.4%).**

5.3   Safety of care

5.3.1   Post-treatment mortality (G-1)

Short-term mortality is a marker of the quality and safety of the therapeutic care provided. Treatment should only be offered to patients for whom the benefits are likely to balance the risks. All treatments should be provided in a safe environment so that toxicity and mortality are as low as possible.[87]

a)   Post-operative mortality

National results

Overall, the proportion of patients who died within 30 days after surgery with curative intent was of 2.2% in Belgium, which is below the target defined by the experts (<5%). The 60- and 90-day mortality was 3.4% and 4.6%, respectively, which is also relatively low. There were some differences in the post-operative mortality between anatomic sites: the 30-day mortality was higher among patients with laryngeal SCC (2.8%) and lower among those with hypopharyngeal SCC (1.3%), while the inverse was true for the 90-day

mortality (4.0% for laryngeal and 5.3% for hypopharyngeal SCC) (Appendix 7.3.1, Table 133). However, given the low number of events (deaths) in the hypopharyngeal group, caution is needed in interpreting these results. Also, as expected, the 30-, 60- and 90-day post-operative mortality was higher among males and increased with age, combined stage, poor performance status, previous inpatient bed days, and comorbidity.

International comparison reveals that lower 30-day mortality was reported in other countries: between 0% and 0.9% (in 2014-2015 and 2016-2017, respectively) in Scotland and between 1.6% and 2.1% (in 2013-2014 and 2009-2012, respectively) in England (Appendix 7.3.1, Table 137).[87, 107-109] Regarding the 90-day post-operative mortality, lower probabilities were also reported in Scotland (0.9% in 2016-2017) and in England (2.4% in 2013-2014), compared to Belgium (4.6% in 2009-2014).[87, 108]

Comparison between centres

The funnel plot illustrates that the variability in 30-day post-operative mortality between surgical centres ranged between 0% and 25%, with one centre at the 99% border and two at the 95% border (Figure 17, left side). In order to take differences in patient case mix between centres into account, adjusted Odds Ratios per centre were calculated (Figure 17), right side). This graph shows some variability in the risk of 30-day post-operative mortality between surgical centres, but there is no clear pattern with surgical centre volume. In fact, approximately half of the centres showed an increased risk of mortality (OR>1.0) compared to the average centre (value of 1.0) and the other half a decreased risk (i.e. better survival; OR<1.0), yet the confidence intervals of all but one centre contain the value 1.0 (so only one centre with a significantly higher risk of mortality). While only centres with at least thirty patients assigned are presented in the forest plot, patients from smaller centres did contribute in the estimation of the case mix parameters. For the volume-outcome analysis, we refer to section 5.5.

Figure 17 – Crude 30-day post-operative mortality by surgical centre and adjusted* Odds Ratios by surgical centre (2009-2014)
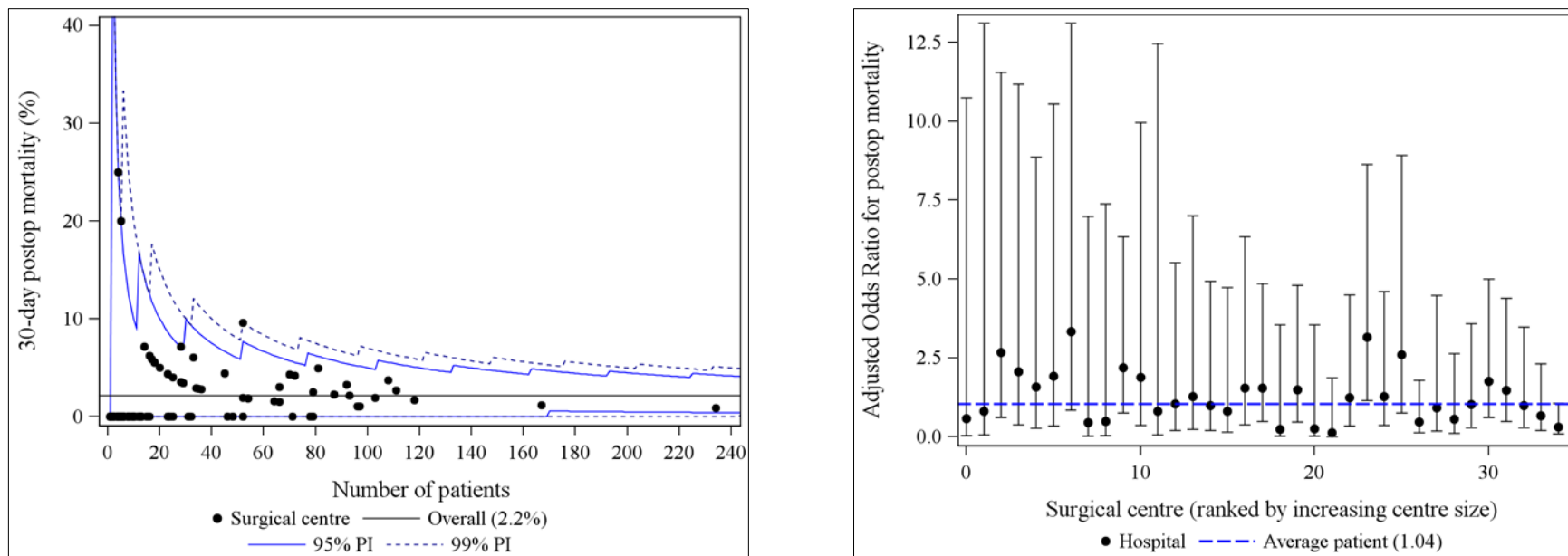
Note to the funnel plot (left): 96 centres reported; 7 patients are not represented as they could not be assigned to a surgical centre.
Note to the forest plot (right): 36 centres reported;
*: adjusted for the following case-mix variables: gender, age, WHO performance status, combined stage, anatomic localisation, number of previous inpatient bed days and Adapted Charlson Comorbidity Index ; value 1.0 represents the average centre and the dashed blue line is the OR for the average patient. The centres are ranked according to the number of patients assigned to them: from smallest (left) to largest (right). The vertical lines represent the 95% CI of the centre OR estimates. For 60 out of the 96 surgical centres, no adjusted OR could be calculated as their volume was too small (i.e. less than 30 patients over the six year period); they are therefore not displayed. Yet, for the estimation of the model, these small centres were grouped into one virtual centre, so that these patients could contribute in the estimation of the adjustment parameters. This grouped virtual centre is not shown in the forest plot.
Source: BCR – IMA

Key Points

- **Mortality within 30, 60 and 90 days after surgery with curative intent in HNSCC patients was 2.2%, 3.4% and 4.6%, respectively, which is below the target (<5% for 30-day mortality);**

- **The post-operative mortality was higher among males and increased with age, performance status, combined stage, previous inpatient bed days and comorbidity;**

- **There were variations according to anatomic sites: while patients with laryngeal cancer had the highest 30-day post-operative mortality risk (2.8%) compared to other anatomic sites, they had the lowest 90-day post-operative mortality risk (4.0%).**

b) Post-radiotherapy mortality

National results

Overall, the proportion of patients who died within 30 days after radiotherapy with curative intent was of 4.0% in Belgium, which is below the target defined by the experts (<5%; Appendix 7.3.1, Table 134). The 60- and 90-day mortality was 5.5% and 7.5%, respectively. While the post-radiotherapy mortality seemed to double between 30-day and 90-day for each anatomic site, oral cavity cancers showed the highest mortality (6.6% and 14.7%, respectively for 30- and 90-day mortality), followed by oropharyngeal (4.4% and 7.5%), hypopharyngeal (4.9% and 9.6%), and laryngeal (2.6% and 4.8%) cancers (Table 134). So, globally, oral cavity cancers showed the highest 90-day mortality after both surgery and radiotherapy treatments. Also, as for post-operative mortality, the 30-, 60- and 90-day post-radiotherapy mortality increased with age, combined stage, poor performance status, previous inpatient bed days, and comorbidity. However,

differences between genders were lower for 30-day post-radiotherapy mortality than for post-operative mortality.

These national results for 30-day mortality after radiotherapy are good, still they are higher than those reported in other countries: between 0.9% and 1.2% (in 2016-2017 and 2014-2015, respectively) in Scotland and 1.3% (in 2013-2014) in England (Appendix 7.3.1, Table 137).[87, 107, 108] Lower proportions were also reported in Scotland (0.9% in 2016-2017) and in England (3.6% in 2013-2014) regarding the 90-day post-radiotherapy mortality.[87, 108]

Compared to post-operative mortality, post-radiotherapy mortality was higher; this is also observed in the international literature (Appendix 7.3.1, Table 137). For instance in the USA, patients with advanced-stage laryngeal cancer who received nonsurgical therapy (CRT or RT) had a statistically significant increased risk of mortality, compared to those receiving total laryngectomy.[110] That may be explained by patient selection (more ''curable'' or ''healthier'' patients may be offered surgical therapy over nonsurgical therapy) or toxicity of the different treatment options.

Comparison between centres

The funnel plot of 30-day post-radiotherapy mortality shows that the variability between radiotherapy centres ranged between 0% and 8% (Figure 18, left side). No centres fell outside the 99% prediction intervals. Also from the forest plot with the Odds Ratios adjusted for case-mix, some variability between radiotherapy centres can be observed (Figure 18, right side). In this graph, two centres were not displayed because the number of patients they treated was too small. For the volume-outcome analysis, we refer to the 'volume outcome' chapter in the report (see section 5.5).

Figure 18 – Crude 30-day post-radiotherapy mortality by radiotherapy centre and adjusted* Odds Ratios by radiotherapy centre (2009-2014)
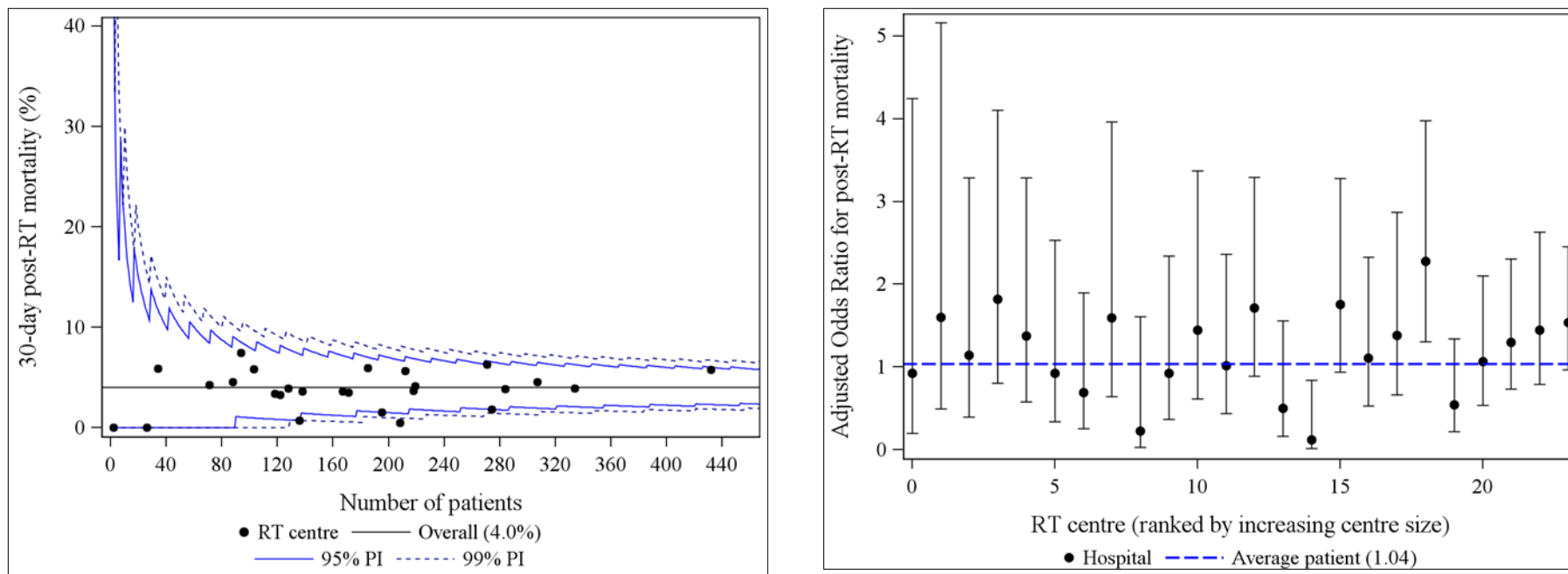
Note to the funnel plot (left): 26 centres reported; 6 patients are not represented as they could not be assigned to a RT centre.

Note to the forest plot (right): 24 centres reported;

*: adjusted for the following case-mix variables: gender, age, WHO performance status, combined stage, anatomic localisation, number of previous inpatient bed days and Adapted Charlson Comorbidity Index ; value 1.0 represents the average centre and the dashed blue line is the OR for the average patient. The centres are ranked according to the number of patients assigned to them: from smallest (left) to largest (right). The vertical lines represent the 95% CI of the centre OR estimates. For 2 out of the 26 radiotherapy centres, no adjusted OR could be calculated as their volume was too small (i.e. less than 30 patients over the six year period); they are therefore not displayed. Yet, for the estimation of the model, these small centres were grouped into one virtual centre, so that these patients could contribute in the estimation of the adjustment parameters. This grouped virtual centre is not shown in the forest plot, although it contributes in the calculation of the average patient OR.

Source: BCR – IMA

Key Points

- **Mortality within 30, 60 and 90 days after radiotherapy with curative intent in HNSCC patients was 4.0%, 5.5% and 7.5%, respectively, which is below the target (<5% for 30-day mortality) but higher than post-operative mortality (2.2%, 3.4%, 4.6%, respectively);**

- **The post-radiotherapy mortality increased with age, performance status, combined stage, previous inpatient bed days, and comorbidity and was higher for oral cavity cancers.**

5.4 Observed and relative survival

5.4.1 The 1, 2 and 5-year observed and relative survival after a diagnosis of SCC of the head and neck (G-2)

National results

Survival in HNSCC patients at one year after diagnosis is estimated to be about[i] 77% and decreases to about 50% at 5 years (Appendix 7.4.1, Table 138). The highest survival probability is observed among patients with laryngeal SCC (83.8% and 60.6%, at 1 and 5 years respectively), and the lowest in patients with hypopharyngeal SCC (65.6% and 30.7%, respectively). This may in part be explained by the fact that the majority (89.8%) of patients with hypopharyngeal SCC were diagnosed with an advanced stage (cIII-IV), while in the laryngeal SCC group, this was the case for 46.5% of patients (see Appendix 6.1, Table 79). Overall, the median survival time for the HNSCC population was 4.8 years, ranging from 2.0 years for patients with hypopharyngeal SCC to 8.0 years for patients with laryngeal SCC. The relative survival proportions (78.2% and 55.0%, at 1 and 5 years respectively) were comparable to the observed survival probabilities,

pointing out that in this population the probability to die is mainly attributable to the SCC (Appendix 7.4.1, Table 138).

Women had a better than average survival and the difference between women and men became more pronounced with longer follow-up time. Similarly, younger patients, asymptomatic patients (WHO performance status 0), patients with fewer comorbidities and those with a lower combined stage had a better prognosis (Appendix 7.4.1, Table 138 and Figure 35). Interestingly, patients who had been admitted in hospital for 1-5 days in the year preceding the diagnosis had a better chance of survival than patients who had not been in hospital at all (Appendix 7.4.1, Figure 35).

As was discussed in section 3.3.5, neither the BCR nor the IMA – AIM database contains data on other well-established risk factors which are also prognostic factors, e.g. HPV infection (head and neck cancer related tumours of HPV infection, e.g. tongue base, tonsil and oropharynx, have a better prognosis compared with the other H&N sites), alcohol consumption, smoking (which has also a substantial impact on treatment efficacy) and the socio-economic background of the patient (survival is substantially higher in more affluent men than in the more deprived).[80-84]

Comparing the observed and relative survival rates with the results from other countries is challenging, as in some publications (e.g. the Thuringia study) the results for the whole study population of head and neck cancers also included cancers of other anatomic locations (e.g. the lip with a known better prognosis) and/or other than SCC (Appendix 7.4.1, Table 144).[111] In addition, previously it has been denoted that differences in anatomical distribution between countries may explain a substantial portion of the survival differences by country for patients with head and neck cancers. Actually, anatomic sub-sites are important determinants of prognosis in head and neck cancer: among mouth–pharynx sites, hypopharynx, base of tongue, lateral and posterior wall of the oropharynx are characterised by

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i   These percentages are estimates. These cannot always be taken as the effective fraction of patients that survived if there is censoring before a given time. In this patient group, for instance, 25% of the patients got censored before 4.1 years.

relatively poor survival, while among laryngeal sites, the supraglottic and subglottic sub-sites have poor survival.[7] Due to varying risk factor prevalence, the distribution of sub-sites in European countries is not homogeneous. For example, the incidence of oral cavity and oropharyngeal cancers is lower in the United Kingdom (UK), Ireland and the Northern countries while it is higher in the Eastern and Southern European countries.[112, 113] Last but not least, as was mentioned before, in this study certain patient groups (among others patients with multiple tumours) were deliberately excluded from the study, which also calls for a careful comparison with other studies (see section 3.1.1).

De Ridder et al. (2017) reported on 2 094 SCC patients, diagnosed in 2008 in the Netherlands (Cancer Registry data).[114] For all four anatomic sites, the 5-year observed survival was higher in the Dutch population compared to the Belgian study group (Appendix 7.4.1, Table 144). The differences between the Netherlands and Belgium were less pronounced in another Dutch study, reporting relative survival rates for patients diagnosed with SCC between 2007 and 2011 (Cancer Registry data, Appendix 7.4.1, Table 145).[115] Yet, the most recent available publication from EUROCARE, the largest cooperative study of population-based cancer survival in Europe (www.eurocare.it), on head and neck cancers reports data from 1999-2007, which is before the time frame of the present study.[7]

Comparison between centres

The 3 518 patients who underwent surgery as their main treatment, were treated in 96 centres (Figure 19, Table 5). Half of the surgical centres treated seventeen HNSCC patients or less over the six year study period. Only three centres treated more than 150 patients over the six year study period (or in other words, on average at least two patients per month). Less than 10% of centres fell outside the funnel 99% prediction interval.

Figure 19 – Distribution of the number of surgically treated HNSCC patients by surgical centre and their unadjusted 5-year observed survival by surgical centre (2009-2014)
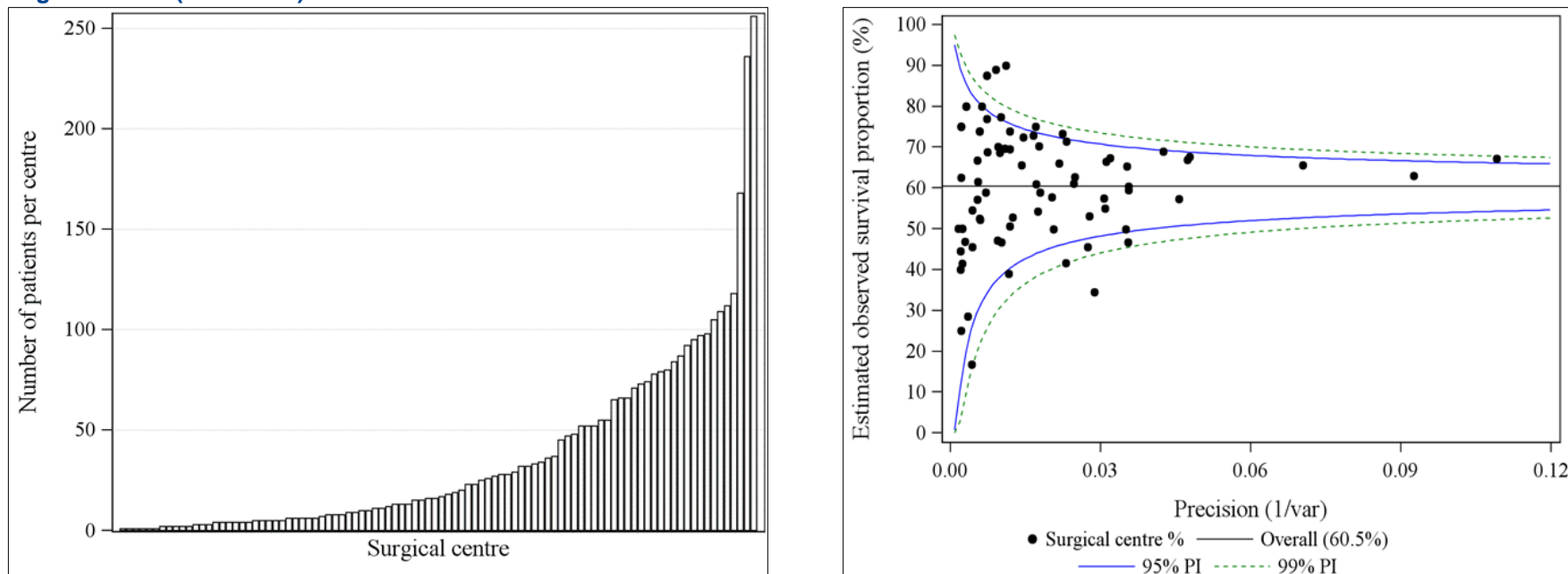
Note to the distribution figure (left): 96 centres reported;
Note to the funnel plot (right): 79 centres reported; to quantify the degree of heterogeneity among centres, the reciprocal of the estimated effect variance (i.e. precision) was used instead of the volume (as was done for the other QIs); in general, larger centres have higher precision and thus have high X-axis values, while small centres have low X-axis values; for eight patients no surgical centre could be assigned and they are not shown in the funnel plot, yet they do contribute to the overall outcome; seven hospitals are not presented in the funnel plot, as they have no patients with a follow-up of at least 5 years; ten hospitals are not presented in the funnel plot as their survival estimate is 0 or 100%, in which case the precision does not exist.
Source: BCR – IMA

Table 5 – Surgical centre size distribution (2009-2014)

Total number of centres	Total number of patients	Min	Q1	Median	Q3	Max
96	3 510	1	5	16.5	53	256

Source: BCR – IMA

Treatment of the 4 660 patients who had radiotherapy as their main treatment, was distributed among all Belgian radiotherapy centres (Figure 20, Table 6). Twelve centres treated on average less than two HNSCC patients a month. The number of centres that fell outside the 99% prediction intervals was rather limited, but more than one third of the centres fell outside the 95% intervals. Yet, it has to be mentioned that these results only reflect the 9 245 HNSCC patients who met the inclusion criteria; for methodological reasons 3 511 patients (including patients with multiple tumours) were excluded from the study (see section 3.1.1).

Figure 20 – Distribution of the number of patients who had primary radiotherapy by RT centre and their unadjusted 5-year observed survival, by radiotherapy centre (2009-2014)
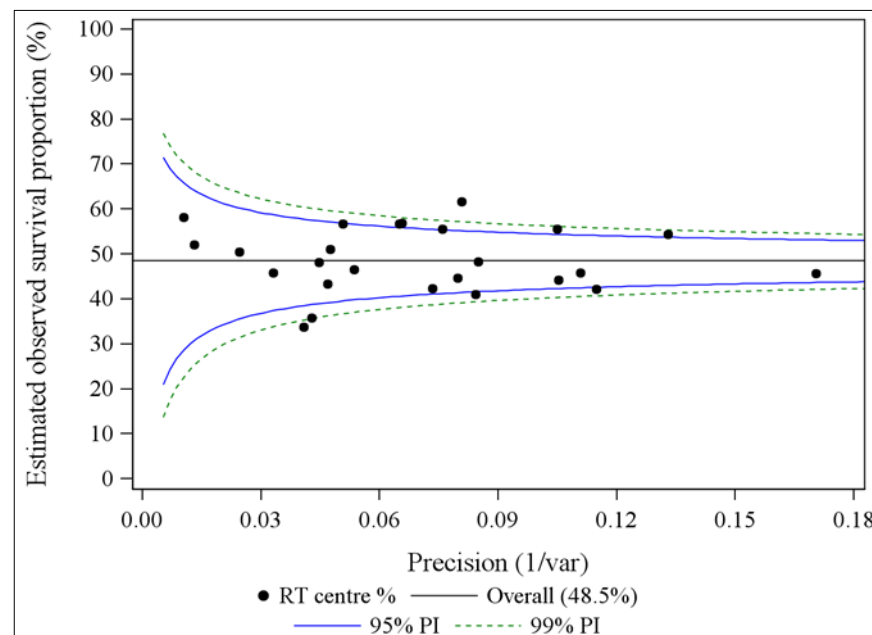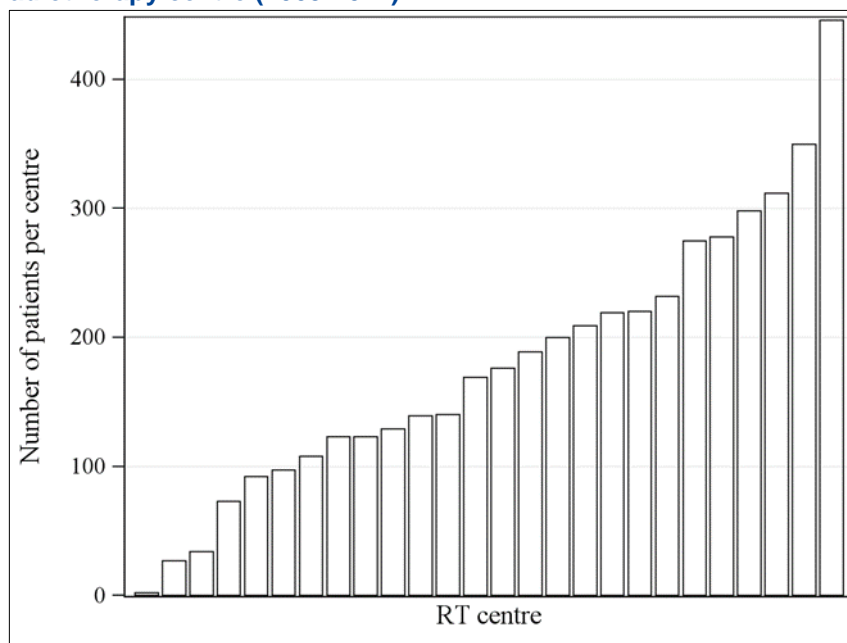
Note to the distribution figure (left): 26 centres reported.
Note to the funnel plot (right): 25 centres reported (one centre not shown as it only treated 2 patients); to quantify the degree of heterogeneity among centres, the reciprocal of the estimated effect variance (i.e. precision) was used instead of the volume (as was done for the binary QIs); in general, larger centres have higher precision and thus have high X-axis values, while small centres have low X-axis values; for six patients no RT centre could be assigned and they are thus not represented in the funnel plot, yet they do contribute to the overall outcome; one hospital is not presented in the funnel plot as its survival estimate is 0 or 100%, in which case the precision does not exist.
Source: BCR – IMA

Figure 21 – Estimated centre Hazard Ratio adjusted for case-mix, by surgical centre and radiotherapy centre (2009-2014)
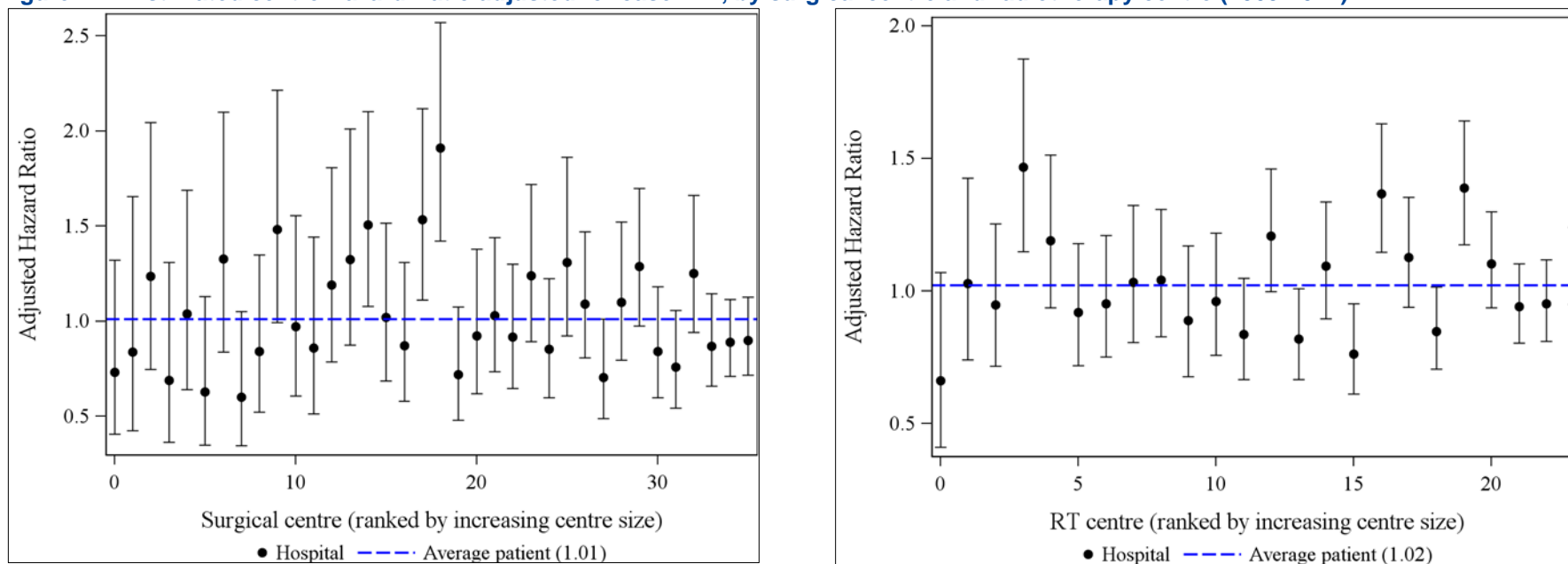
Notes: Value 1.0 represents the average centre and the dashed blue line is the HR for the average patient (which equals the weighted sum of all centre HR, with the number of patients per centre as weight). The centres are ranked according to the number of patients assigned to them: from smallest (left) to largest (right). A HR which is lower than 1.0, indicates a lower hazard (or instantaneous risk) to die, and thus a higher survival. When the vertical lines, which represent the 95% CI on the centre HR, include value 1.0 (dashed line), the HR of that centre is not statistically significantly different from the average centre (average patient).

For 60 out of 96 surgical centres and 2 out of 26 RT centres, no adjusted HRs could be calculated as their volume was too small (i.e. less than 30 patients over the six year period); they are therefore not displayed. Yet, for the estimation of the model, these small centres were grouped into one virtual centre, so that these patients could contribute in the estimation of the adjustment parameters. This grouped virtual centre is not shown in the forest plot, although it contributes in the calculation of the average patient HR.

Source: BCR – IMA

Table 6 – RT centre size distribution (2009-2014)

Total number of centres	Total number of patients	Min	Q1	Median	Q3	Max
26	4 660	2	108	172.5	232	446

Source: BCR – IMA

Key Points

- **Survival in HNSCC patients at one year since diagnosis is estimated to be about 75% and decreases to about 50% at 5 years;**

- **The highest survival is observed among patients with laryngeal SCC (83.8% and 60.6%, at 1 and 5 years respectively), and the lowest in patients with hypopharyngeal SCC (65.6% and 30.7%, respectively);**

- **Women, younger patients, asymptomatic patients, patients with fewer comorbidities, patients with a lower combined stage and those who had been admitted in a hospital for 1-5 days in the year preceding the diagnosis, had better survival than average.**

5.5 Association between hospital volume and outcome (V-1)

5.5.1 Introduction

In previous KCE reports the relation between volume and outcome was evaluated for several cancer types.[3-6] Some of these insights were used to write a report on the organisation of care of adults with rare or complex cancers.[14] For HNSCC in particular, it was recommended that these patients should only be treated in reference centres, with a sufficient number of patients treated per year to maintain a high level of expertise. During the development of both clinical guidelines that preceded this report, the volume-outcome relationship was also raised by the guideline development group as an important issue when it comes to quality of care.[22, 23]

The current analyses have two aims:

1. To evaluate the association between hospital volume and **observed survival** in HNSCC patients, adjusted for a range of patient and tumour characteristics;

2. To evaluate the association between hospital volume and **30-day post-treatment mortality** in HNSCC patients, adjusted for a range of patient and tumour characteristics.

5.5.2 Methods

Statistical models

Observed survival

Log-rank tests were used to compare the observed survival curves between low and high hospital volume categories.

The association between hospital volume and observed survival since diagnosis was assessed with Cox proportional hazard models. The survival analysis was confined to the 0-5 year time interval since diagnosis, by administrative censoring patients with a longer follow-up at 5.05 years. The analyses were adjusted for potential confounders by adding them as covariates in the models. Potential confounders were: gender, age group at diagnosis, WHO performance status, combined stage, Adapted Charlson Comorbidity Index and the number of inpatient bed days during the year before diagnosis (see section 3.3.5). Additionally, anatomic site was added as an adjustment covariate when all HNSCC tumours were considered together. Missing observations for a covariate (e.g. missing values for the Adapted Charlson Comorbidity Index), were assigned to an extra-category

'missing' (no imputation techniques were applied). The number of missing observations for each confounder is presented in Appendix 7.5.1, Table 146. In order to account for the clustering of patients into hospitals, hospital was added as a random term to the Cox regression models.

As there is so far **no consensus** regarding the **cut-off used to define 'high' and 'low' volume** hospitals, treatment volume was treated as a continuous covariate in the survival models.[116] A plot of the Martingale residuals of the model containing all adjustment variables (but not volume) versus main treatment volume was inspected to decide on the functional form of main treatment volume. These residual plots revealed a decreasing trend with increasing volume for the low-volume range, which flattened off at higher volumes. A piecewise linear model with two sections was therefore adapted, with both linear pieces joined at a knot. A range of plausible values for the knot was compared and the one giving the lowest Akaike Information Criterion (AIC) was selected for the final model. These knots should not be interpreted as 'set in stone'; they are just indicative, with the 'true' underlying value in their neighbourhood.

More technical details on how non-proportionality was evaluated and handled are provided in Appendix 7.5.1.

In sensitivity analyses, the association between observed survival up to 5 years since diagnosis and main treatment, surgery or RT volume was assessed using Cox proportional hazard models. The Hazard Ratio (HR) for surgical/RT volume has been determined for all H&N tumours as well as for the four anatomic sites and the combined stages separately (by adding an interaction term with volume in the model).

30-day post-treatment mortality

Additionally, the association between surgical/RT volume and 30-day post-treatment mortality was assessed using logistic regression models (cf. infra). The Odds Ratio for all-cause death within 30 days since the end of surgery/RT treatment by surgery/RT volume is presented for all H&N

tumours pooled and by anatomic site (by adding an interaction term between volume and anatomic site). The same covariates were added in the models as in the analyses of observed survival.

Again, volume was treated as a continuous covariate in the logistic regression model. A plot of the deviance residuals of the model containing all adjustment variables (but not volume) versus centre volume was inspected to decide on the functional form of volume. Linear associations with volume were used.

Patients assigned to main treatment centre

Patients were assigned to a hospital on the basis of the main treatment they received. If for a patient no treatment was identified in the database, the hospital where the multidisciplinary team meeting (MDT) took place or, if not applicable, the biopsy was billed, was selected as main treatment centre [j]. Out of the 9 245 HNSCC patients, 70 patients could not be assigned to a main treatment centre, leaving 9 175 HNSCC patients for these volume-outcome analyses.

Only patients diagnosed with a unique tumour of the oral cavity, the oropharynx, the hypopharynx or the larynx (squamous cell carcinoma) were taken into account to calculate the volume of the centres.

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[j]   The percentages of patients attributed based on biopsy: oral cavity SCC: 2.1%, oropharynx SCC: 1.6%, hypopharynx SCC: 1.8% and larynx SCC: 2%.

5.5.3   Results

5.5.3.1   Association between hospital volume and observed survival

These analyses were performed in two levels: first we assessed the association between the total volume of each hospital and observed survival, from the perspective of the total institutional experience and reflecting the importance of the multidisciplinary approach in head and neck cancer. In a second level, the association between surgical volume and observed survival on the one hand and radiotherapy volume and observed survival on the other hand were assessed, in line with what is reported in the international literature.

INSTITUTIONAL EXPERIENCE: ANALYSIS BY MAIN TREATMENT CENTRE

In these analyses the volume of each hospital corresponds to the number of HNSCC patients who received their main treatment in that particular hospital during the six year study period.

The association between hospital volume and observed survival up to 5 years was first assessed for all HNSCC patients together. In subsequent analyses the association per anatomic site was assessed. When a significant association was observed, the potential interactions between volume and anatomic site (when all HNSCC were considered) or combined stage (for all HNSCC and the anatomic site subgroups) were explored and HRs between anatomic sites or combined stages were estimated. In both sections, crude observed survival proportions for specific categorical volume groups at 1, 2 and 5 years are also provided.

All HNSCC patients together

The 9 175 HNSCC patients included in these volume-outcome analyses, were treated in 99 different centres (Table 7). The median treatment centre volume was 25 unique patients over the six year period (or in other words: half of the centres treated four HNSCC patients or even less per year); a quarter of the centres (Q1) treated not more than ten patients over the six year period, or less than two per year (see Table 7, Figure 22).

Figure 22 – Distribution of HNSCC patients by main treatment centre (2009-2014)
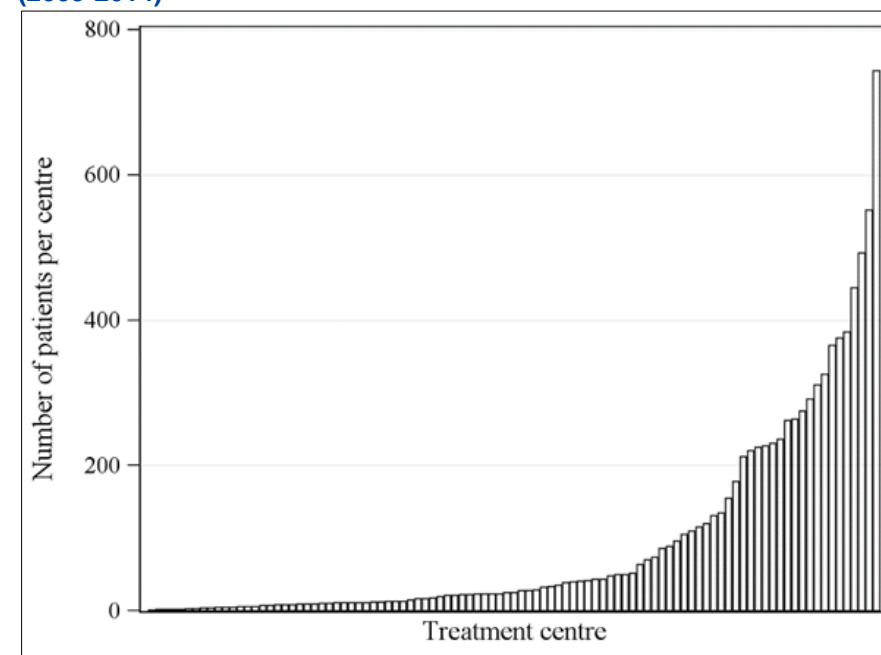
Source: BCR – IMA

Table 7 – Distribution of the number of HNSCC patients by main treatment centre over the six year study period (2009-2014)

Total number of centres	Total number of patients	Minimum	Q1	Median	Q3	Maximum
99	9 175	1	10	25	115	744
Average number per year	1 529	<1	1.6	4.2	19.2	124

Q: quartile
Source: BCR – IMA

In order to distinguish low versus high-volume centres for the unadjusted (i.e. not taking the case-mix of hospitals into account) survival analyses, the break point ('knot') defined in the Cox proportional hazard model was used, i.e. 120 patients over the six year study period. This break point is illustrated in Figure 23 (and explained in the following paragraph). Patients who were treated in high-volume centres had a statistically significantly higher estimated survival probability (p<0.0001, not adjusted for patient case-mix) than patients who were treated in low-volume centres (78.7% versus 70.0%, respectively at one year since diagnosis), and this difference decreased with longer follow-up time (50.2% and 46.3% at 5 years, respectively; Table 8). The median survival of patients treated in high-volume centres was 1.1 year longer than their peers treated in low-volume centres (5.1 versus 4.0 years).

In order to take the case-mix of hospitals into account, a Cox proportional hazard model was developed. This model is visualised in Figure 23, showing the evolution of the predicted Hazard Ratio according to main treatment volume: the break point or optimal knot for the piecewise linear volume association is situated at 120 patients over the six year period. The hazard to die of any cause decreased on average with 0.4% per increase of one additionally assigned patient below 120 assigned patients over the six year period (HR: 0.996, 95% CI: 0.995 - 0.998, p<0.0001). Once the number of assigned patients is higher than 120 patients, there was no further decrease in hazard (HR: 1.000, 95% CI: 1.000 - 1.001, p=0.67). Over the six year study period, 76 centres treated 120 or even less HNSCC patients, while 23 centres could be considered as high-volume centres. The reference hazard is set to a main treatment hospital volume of more than 120 patients.

This model was extended to estimate the HR for main treatment volume **per anatomic subsite**, by adding the interaction term between the site and the volume covariates. A significant association between volume and observed survival was revealed for patients with oropharyngeal, hypopharyngeal and laryngeal SCC: the hazard to die of any cause decreased on average with 0.6 - 0.7% per increase of one additionally treated patient below the knot of 120 assigned patients without any further gain for larger treatment volumes (Appendix 7.5.1, Table 147). No significant association was observed for oral cavity SCC.

A similar analysis was performed by combined stage, which revealed no significant association between main treatment volume and observed survival (Appendix 7.5.1, Table 148). However, when combining stages III and IVA-B, there was a significant difference in observed survival according to main treatment volume, which is presented in Appendix 7.5.1, Figure 36.

Figure 23 – Cox proportional hazard model with indication of the break point
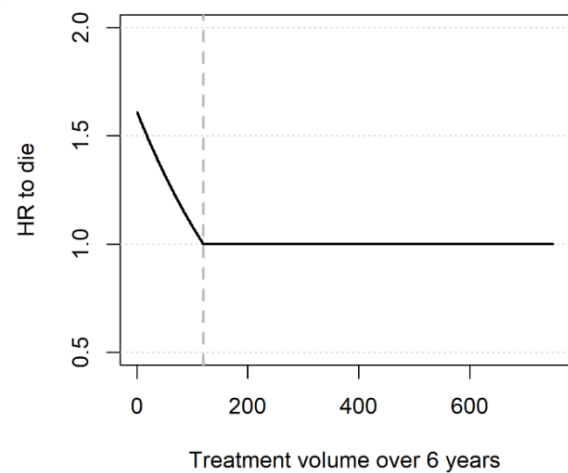
Source: BCR – IMA

Table 8 – 1-, 2-, and 5-year unadjusted observed survival and median observed survival for all HNSCC, by main treatment volume (2009-2014)

	N centres	N patients	1-year	2-year	5-year	Median observed survival (years)	p-value*
				Observed survival (%, 95% CI)			
Overall	99	9 175	76.7 (75.8, 77.5)	65.1 (64.1, 66.0)	49.3 (48.3, 50.4)	4.8	
Main treatment volume							<0.0001
≤ 120 patients over 6 years	76	2 135	70.0 (68.0, 71.9)	60.2 (58.1, 62.2)	46.3 (44.1, 48.5)	4.0	
> 120 patients over 6 years	23	7 040	78.7 (77.7, 79.6)	66.6 (65.4, 67.7)	50.2 (49.0, 51.5)	5.1	

*Source: BCR – IMA; * p-value applies to the log-rank test between the survival curves.*

ANALYSES BY TREATMENT TYPE

Surgical volume

In these analyses the volume of each hospital corresponds to the number of HNSCC patients who had surgery (whether or not in combination with adjuvant therapy) as their principal treatment in that particular hospital during the six year study period.

The 3 474 HNSCC patients included in these surgical volume-outcome analyses were treated in 96 different centres (Table 9). The median surgical centre volume was seventeen patients over the six year period, meaning that half of the centres performed surgery in fewer than 3 HNSCC patients per year.

Table 9 – Distribution of the number of HNSCC patients by surgical treatment centre over the six year study period (2009-2014)

Total number of centres	Total number of patients	Minimum	Q1	Median	Q3	Maximum
96	3 474	1	5	16.5	53	256
Average number per year	579	<1	<1	2.8	8.8	42.7

Note: 37 IVC patients and 7 patients who could not be assigned to a hospital were omitted from the analysis.
Q: quartile
Source: BCR – IMA

Results from the Cox regression models, taking the case-mix of hospitals into account, showed no statistically significant association between surgical centre volume and overall survival among patients with HNSCC (HR: 0.999, 95% CI: 0.998 - 1.000, p=0.23). However, there was a significant association between surgical volume and overall survival for patients with laryngeal SCC: the hazard to die of any cause decreased with 0.2% per increase of one additional patient with HNSCC who had surgery (see Appendix 7.5.1,

Table 161). No significant association was observed for oral cavity, oropharyngeal or hypopharyngeal SCC. Additionally, a similar analysis was performed by combined stage, which only revealed a significant association between surgical volume and observed survival for combined stage I and III (Appendix 7.5.1, Table 162).

Radiotherapy volume

In these analyses the volume of each hospital corresponds to the number of HNSCC patients who had primary RT (whether or not in combination with another treatment modality) as their principal treatment in that particular hospital during the six year study period.

The 4 539 HNSCC patients included in these RT volume-outcome analyses were treated in all 26 Belgian RT centres (Table 10). The median RT centre volume was 169 patients over the six year period (28 patients or less per year) and a quarter of the centres treated fewer than 103 patients over the six year period (17 patients per year).

Table 10 – Distribution of the number of HNSCC patients by radiotherapy treatment centre over the six year study period (2009-2014)

Total number of centres	Total number of patients	Minimum	Q1	Median	Q3	Maximum
26	4 539	2	103	169	219	432
Average number per year	756.5	<1	17.2	28.2	36.5	72

Note: 121 IVC patients and 6 patients who could not be assigned to a hospital were omitted from the analysis.
Q: quartile
Source: BCR – IMA

There was no statistically significant association between RT centre volume and overall survival among patients with HNSCC (HR: 1.000, 95% CI: 0.999 - 1.001, p=0.61). Analyses by anatomic site and combined stage revealed no interaction between RT centre volume and anatomic centre or combined stage on overall survival (Appendix 7.5.1, Table 163 and Table 164).

5.5.3.2 Association between hospital volume and 30-day post-treatment mortality

SURGICAL VOLUME

The analyses are based on 3 472 HNSCC patients; in comparison to the survival analyses two additional patients had to be excluded as they were censored within the 30 days' time span after surgery.

Taking the case-mix of hospitals into account, the logistic regression model showed that the 30-day post-operative mortality decreased non-significantly with increasing surgical centre volume (OR: 0.997, 95% CI: 0.993 - 1.001, p=0.09).

The extended model to estimate the OR for post-treatment mortality versus surgical centre volume per anatomic subsite (by adding an interaction term between the site and the volume covariates) revealed no significant association between volume and the 30-day post-operative mortality (Appendix 7.5.1, Table 165).

Note that in these analyses, clustering of patients into hospitals could not be performed, due to the low number of deaths, the large number of hospitals and the many low-volume centres.

RADIOTHERAPY VOLUME

Again, in comparison to the survival analyses, two additional patients had to be excluded, leaving 4 537 HNSCC patients for the analyses.

Adjusted results from the logistic regression models showed no statistically significant association between RT centre volume and the 30-day post-RT mortality (OR: 1.001, 95% CI: 0.999 - 1.003, p=0.23); similarly, no associations were found when the analyses were performed by anatomic subsite (Appendix 7.5.1, Table 166).

5.5.4 Discussion

The results of the analyses taken the total institutional experience into account indicate unequivocally that HNSCC patients who were treated in high-volume centres had a statistically significantly higher chance to survive than patients who were treated in low-volume centres. The median survival of patients treated in high-volume centres was 1.1 year longer (5.1 versus 4.0 years). This observation was further confirmed in analyses taking the case-mix of hospitals into account: for patients treated in centres with a HNSCC volume smaller than 20 patients a year (120 over six years), the hazard to die of any cause decreased on average with 0.4% per increase of one additional patient. A similar volume outcome relationship was also observed in the analyses restricted to patients with oropharyngeal, hypopharyngeal and laryngeal SCC, but not for patients with oral cavity SCC.

The results are **supported by the international literature**. In a recent systematic review, in which the results of five studies evaluating hospital volume and long-term overall survival for head and neck cancer patients were meta-analysed, it was clearly demonstrated that high-volume hospitals are predictors of better overall survival (pooled random effects model HR: 0.886, 95% CI: 0.820 - 0.956).[117] Primary studies performed in the USA, Canada and the Netherlands and published after that systematic review were also unisonous: patients with head and neck cancer who were treated in high-volume centres had significantly improved overall survival.[114, 118, 119]

Several **hypotheses explaining this volume-outcome association** have been suggested. Birkmeyer et al. suggested that for high-risk surgical procedures with relatively limited hospital stay, volume outcome associations can largely be explained by surgeon volume. However, this is different for procedures which require an extended length of stay, intensive care unit admission, and/or multidisciplinary in-patient or out-patient care, which are more likely to be affected by plenty of hospital volume-related variables. For these procedures, the volume-outcome relationship can largely be explained by hospital volume.[120] For these reasons, it is not surprising that for head and neck cancer surgery, which not only requires multidisciplinary care delivered by a large team but in many cases also an extended hospital stay, there is a relationship between hospital volume and

outcome. Thanks to their expertise and experience, healthcare professionals in high-volume centres can quickly identify and treat perioperative complications as well as judiciously transfer patients to the intensive care unit or long-time monitoring, and/or supportive therapies.[121, 122] A Canadian study in HNSCC patients illustrated that in high (surgeon and hospital surgical) volume centres, adherence rates to guideline-recommended processes of care in the surgical management of patients with head and neck cancer were higher. Still, the authors noted that even in these centres there was room for improvement.[90] Likewise, Wuthrick and co-workers reported higher radiotherapy protocol deviations in low-volume centres [k], contributing (in part) to the lower survival probabilities in patients with head and neck cancer observed in these centres and suggesting that experienced providers likely execute superior treatment plans and may better support patients through treatment.[119] A large international phase III study in patients with advanced head and neck cancer indicated that the probability of receiving poor-quality RT was most highly correlated with the number of patients enrolled at each centre: significant non-compliant radiation plans were observed in 5.4% of cases in sites enrolling twenty or more patients, whereas it was reported in 29.8% of sites contributing fewer than five patients and non-compliance in its turn was associated with reduced survival.[123]

Yet, our additional analyses assessing the association between **surgical centre volume** and overall survival on the one hand and between **RT centre volume and overall survival** on the other revealed **no statistically significant association**, which is in contrast with the findings from other recent studies.[114, 118, 124]

The results of the present analyses **support** the '**Concrete proposals formulated by the Head and Neck multidisciplinary working group**' which were composed within the frame of the KCE study 'Organisation of care for adults with rare cancers and cancers with complex diagnosis and/or

treatment'.[14, 125] The authors recommended to concentrate the care for patients with head and neck cancer in reference centres, where a multidisciplinary team of experts (in among others pathology, radiology, nuclear medicine, head & neck surgery, radiation oncology, medical oncology) dedicated to head & neck cancer either exclusively or with a major part of their working time typically manage a large number of patients per year.

Last but not least some remarks have to be made. First, the treatment of HNSCC is extremely dispersed in Belgium with the difference in the number of patients treated in low-volume centres and high-volume centres being relatively small compared to other countries. For example, in the Dutch study, hospital volume varied between 65 and 417 patients yearly, while in the present study total hospital volume ranged between 1 and 124 patients per year.[114] Consequently, studying volume-outcome relationships in Belgium is difficult, with small effect sizes to be found at most. This may (in part) explain why we did not observe a significant association between surgical and RT centre volume and observed survival. Furthermore, it is important to realise that some of the centres that are categorised as high-volume centres are in reality a cluster of recently merged low-volume centres. These merged centres may still act and manage patient care as individual (low-volume) entities without centralising some care aspects (e.g. diagnosis and management of rare and complex cancers), with each low-volume entity still taking care of a small number of patients. Patients taken care of in these so-called high-volume centres clearly miss the benefits of the real high-volume centres. From the administrative database it was not possible to identify those so-called high-volume centres. Yet, it can be hypothesized that if several high-volume centres are in reality still working as clusters of low-volume entities, this may have attenuated the differences in survival probabilities between high and low-volume centres.

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k   As a surrogate for institutional expertise, institutional accrual volume to 21 HNC clinical trials conducted by the RTOG during the 5-year period (July 30, 1997- to July 29, 2002) immediately before the activation of RTOG 0129 was used.

Another important limitation of this study is that not all important confounding factors could be taken into account in the analyses, as they were not available in the database. To name only some: socio-economic status, HPV status, smoking behaviour, alcohol abuse.

The analyses were based on 9 245 patients who were diagnosed with a single HNSCC residing in Belgium in the 2009-2014 period. As is explained in the section 3.1.1, 3 511 patients had to be excluded for methodological reasons (i.e. patients with multiple invasive tumours, patients for whom no IMA – AIM data or follow-up data were available). Hence, these 3 511 patients were not included in the volume-outcome analyses. The actual number of HNSCC patients seen in Belgian hospitals is thus in reality higher. Yet, for the sake of completeness we evaluated (based on the MDT centre) the distribution of patients with multiple tumours over the centres and observed only 2% more patients with multiple tumours in low-volume centres compared to high-volume centres. Consequently, we estimate that the distribution of patients with multiple tumours is not dependent on the volume of the centre.

The use of an administrative database implied that it was not possible to identify the underlying reasons for the better outcomes observed in the high-volume centres: was it thanks to a higher quality MDT, a more experienced surgeon, radiation oncologist, medical oncologist, intensive care specialist, a more dedicated paramedical team, a better follow-up or the combination of several factors? The format of the administrative database did not allow to analyse the association between surgeon volume and outcome nor the association between radiation oncologist volume and outcome. Neither was it possible to analyse whether there was a difference in quality of life for patients and whether that also had an impact on the survival probability. Additional prospective studies in these fields should further explore these aspects.

Key Points

- **At present the care for patients with head and neck cancers in Belgium is very dispersed over 96 hospitals, half of them treating four or even less HNSCC patients per year;**

- **Survival probabilities were significantly better for patients treated in high-volume centres: the median survival of patients treated in high-volume centres was 1.1 year longer (5.1 versus 4.0 years);**

- **These results support the recommendation to concentrate the management of head and neck cancer patients in reference centres;**

- **The processes of care in those hospitals with better outcomes should be further analysed, so that they can be adopted more widely and lead to a further improvement of the quality of care.**

6 STRENGTHS AND LIMITATIONS

An exhaustive database

One of the major strengths of this study is the fact that the quality of care for patients with HNSCC could be assessed in the large population based database of the Belgian Cancer Registry, covering more than 98% of all cancer cases in Belgium.[126] This led to a study cohort of 9 245 patients diagnosed with a single squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx or larynx between 2009 and 2014. The vital status data were available until 14 December 2017 in the Crossroads Bank for Social Security, allowing a follow-up of at least three years for nearly all patients. The use of an existing database, linked to the IMA – AIM and MZG – RHM database, offered the advantage that all Belgian centres were included (no dependence on the willingness to collaborate) and that no additional registration efforts were needed.

Case-mix adjustment

As was explained before, case-mix adjustment is essential when quality of care is measured and outcomes are compared between providers. Whenever relevant and possible, the following confounders were taken into account: gender, age group at diagnosis, WHO performance status, combined stage, the number of days in hospital during the year preceding the HNSCC diagnosis and the Adapted Charlson Comorbidity Index. A limitation of the study is that no data were available for HPV infection nor for the socio-economic background of the patient, two well-established risk factors in HNSCC. In addition, some comorbidities that are taken into account when (deviations from) the treatment plan are assessed (e.g. insufficient renal function and hearing loss when concomitant platinum-based chemoradiotherapy are considered, see section 3.3.2) are not included in the database, while they may explain (in part) why certain pre-defined targets were not reached.

Intense collaboration with experienced clinical experts

From the very start of this project (the development of the two clinical guidelines) until the very end, this study was performed in close collaboration with clinical experts with profound experience in the diagnosis and treatment of patients with head and neck cancers. Thanks to their input in the selection and the technical elaboration of the quality indicators (e.g. selection of procedure codes, selection of specific patient groups, definition of realistic time frames and targets), their critical reading of the documents and their lasting participation in over 20 meetings during which all chapters were discussed in depth, the quality of the report has been improved and the link with actual clinical practice was preserved.

Individual feedback to hospitals and health care providers

Upon publication of this report, each Belgian hospital will receive from the Belgian Cancer Registry an individual feedback report with its own results for the quality indicators under study, benchmarked to those of all other hospitals (which are kept blinded). The concept is that mirror-information may act as a catalyst for quality improvement in care, which ultimately may lead to a better quality of care offered to patients with head and neck cancer.

But, interpretation of administrative claims data not straightforward

As was already described in section 3.1.1, patients with multiple invasive tumours (N=3 287) were excluded from the analyses, in order to maximally ensure that recorded diagnostic and therapeutic procedures were indeed performed within the frame of the HNSCC under study and not for another malignancy. Yet several other database related issues had to be tackled. The first being the identification of diagnostic and therapeutic procedures (and especially surgical procedures performed with curative intent) in the administrative database, a problem inherent to the use of claims data where one is dependent on the specificity of the description of procedures or procedure labels. Certain procedure labels are extremely vague: some may be performed both outside the oncological context, and within the context of head and neck cancer. Often it was difficult to reveal whether the procedure had been performed either for diagnostic or for therapeutic reasons (e.g. nomenclature codes 258090 – 258101: endoscopic surgery on the larynx: cordopexy, arytenoidectomy, arytenoidopexy). Similar problems were

encountered with the MRI codes: nomenclature codes 459410 – 459421 refer to an MRI of the neck, thorax, abdomen or pelvis, so these codes may refer to MRI within as well as outside the context of head and neck cancer. For radiotherapy, problems arose from the fact that several RT centres invoiced not always according to the instructions issued by RIZIV – INAMI:[41] they did not record each fraction separately and/or the total RT was not always invoiced on the last day of the RT schedule, making it difficult to deduce how many fractions were given, when RT was started (based on which distinction is made between induction and concomitant CRT) or when RT was completed. A check of the database revealed that 81.3% of all RT schemes were recorded in line with the nomenclature; in five RT centres almost none of the RT schemes were invoiced according to the RIZIV-INAMI rules.

Despite an intensive validation study, subsequent checks with hospital discharge data (MZG – RHM) and with pathology reports, we could not obtain an acceptable concordance level for surgical procedures with curative intent for T1-T2 hypopharyngeal SCC (i.e. 88%), which calls for a careful interpretation of these results.

Another aspect that calls for a prudent reading of the results, is the observation that certain nomenclature codes are 'used' for other procedures than the ones intended, due to a lack of proper codes for the procedure that was performed (e.g. because the updates of the nomenclature do not keep pace with current practice) or because the reimbursement provided for the actual procedure is considered too low. This observation was also made and confirmed by clinical experts in a previous KCE report.[127]

In addition, the lack of more detailed clinical information (e.g. function and/or organ sparing characteristics of a surgical procedure, results of diagnostic imaging, resection margins, HPV infection) led to several initially selected QIs not being measurable. Registration of HPV status for oropharyngeal cancers is not mandatory and is currently not included in the standard data set for cancer registration (MDT form for the oncology departments) nor in the data set for the pathologist. Yet, in the near future, it will be possible to assess HPV status since the BCR adopted machine learning techniques to capture the information from the (written) pathology protocols.

Last but not least, diagnostic and therapeutic procedures performed in the contexts of clinical trials are not reimbursed by the sickness funds and hence not included in the administrative data. This may have led to some underestimation in some process QIs.

And how multidisciplinary was the actual care offered?

The database carried some more important limitations. Firstly, it was impossible to reveal whether each individual patient was offered the multidisciplinary approach that is so essential in this patient group. Indeed, the complexity of head and neck cancers, the close proximity of functionally important anatomic structures, the fact that patients are often elderly with medical comorbidities and the early and late toxicities of several treatment options, necessitate a multidisciplinary approach. Several initially selected quality indicators were intended to assess these aspects of care, but due to the unavailability of pertinent data, they could not be elaborated. For example, based on the used database it was not possible to evaluate whether all indicated medical specialties were involved throughout the whole care process, whether patients were referred to a dentist before the start of oncological (radiotherapy) treatment and were offered prosthetic rehabilitation afterwards, whether patients at risk for malnutrition received dietary counselling and nutritional therapy, whether patients were introduced to suitably qualified speech therapists prior to commencing treatment if this treatment was likely to cause problems with chewing, swallowing and/or speech, whether patients who had a radical neck dissection or radiation in this area were offered speech revalidation or whether patients were given psychosocial care.

A proxy for some aspects of multidisciplinary care could have been the registration of multidisciplinary team meetings (MDTs), but as was pointed out previously, these data may somewhat underestimate the real frequency of MDTs (due to among others the reimbursement rules).[85] But more importantly, these data do not reveal whether the MDT was truly dedicated to head and neck cancer, attended by sufficiently experienced medical and paramedical experts and whether it also resulted in a multidisciplinary approach throughout the whole care process.

What about quality of life, functional recovery, patient experiences?

Based on the used administrative data, it was not possible to document patient-reported outcomes or experiences like quality of life, functional recovery, experience with healthcare providers, information and communication, shared decision-making, coordination of care, guidance and support, completion of treatment, follow-up. Likewise, the information on palliative and supportive care in the database was too limited to derive any serious conclusions. Prospective data collection on these aspects would certainly be an asset for future quality monitoring. For that purpose, one can draw inspiration from the Netherlands, where a set of quality indicators including complications, quality of life and patient experiences was established to measure the quality of integrated care for head and neck cancer patients.[128]

Limitations inherent to retrospective analyses of administrative databases

A final remark to be made on the use of administrative databases is that it does not allow the identification of underlying reasons for the better outcomes observed in the high-volume centres. Neither was it possible to analyse whether there was a difference in quality of life for patients and whether that also had an impact on the survival probability. Additional prospective studies in these fields should further explore these aspects.

Deficient reporting to the BCR

An area where there is substantial room for improvement is the quality of data reporting to the BCR. For instance, for 19% of included patients, the WHO performance status was not transferred to the BCR. But more importantly, for 19% of all patients and 22% of operated patients, clinical and pathological stage information respectively was lacking. As was mentioned before, the importance of TNM information cannot be overrated, neither in clinical practice nor in quality assessment. This observation is even more puzzling knowing that cancer stage reporting is one of the legal obligations of the responsible physician of the multidisciplinary meeting to hold the accreditation as oncological care program.[91] Especially low-volume centres perform poorly: 31% of clinical stage and 27% of pathological stage information was missing while the respective proportions in the high-volume centres were 16% and 18%. Could stage reporting be improved when the reimbursement of the MDT discussion and the financing of data managers is linked with the quality of data reporting to the BCR?

7 CONCLUSIONS AND PERSPECTIVES FOR THE FUTURE

Compared to other Central European countries, the age-standardised 5-year relative survival for patients with head and neck cancer was below average: 46.2% compared to a mean of 48.6% for Central Europe.[7]

At present, patients with head and neck cancer are treated in nearly all Belgian acute hospitals. Half of the centres treated four or even less HNSCC patients included in the study per year. Our results reveal that **HNSCC patients who were treated in high-volume centres had a higher chance to survive than their peers who were treated in low-volume centres**. The median survival of patients treated in high-volume centres was 1.1 year longer (5.1 versus 4.0 years). This observation was further confirmed in analyses taking the case-mix of hospitals into account. The dispersion of care does not only have an impact on the quality of care and on the outcomes of care, it also hampers a thorough evaluation of the quality of care. For instance, in the evaluation of 30-day post-operative mortality, no adjusted Odds Ratio could be calculated for 60 out of the 96 surgical centres, as their volume was too small (i.e. less than 30 patients over the six year period). Moreover, the **dispersion of care in HNSCC patients is in reality more pronounced than can be deduced from the administrative database**. As was pointed out above, some of the centres that are categorised as high-volume centres are in reality a cluster of recently merged (low-volume) centres, with each low-volume centre still taking care of a small number of patients. This may have attenuated the differences in survival probabilities between high and low-volume centres. In the same way is RT in Belgium dispersed over 25 'main radiation oncology departments' and 11 'satellite radiotherapy units' (which are affiliated with one of the main centres). However, based on the RIZIV – INAMI licensing codes the distinction between both cannot be made. Hence, all patients who had RT with curative intent were assigned to one of the main RT centres, while in reality they may have been treated in one of the satellite centres.

In line with the 'Concrete proposals formulated by the Head and Neck multidisciplinary working group' which were composed within the frame of the KCE study 'Organisation of care for adults with rare cancers and cancers with complex diagnosis and/or treatment',[14, 125] **the results support the plea for concentration of care for patients with head and neck cancer in reference centres**, where a multidisciplinary team of experts dedicated to head and neck cancer either exclusively or with a major part of their working time typically manage a large number of patients per year.

In addition, the **processes of care in those hospitals with better outcomes should be further analysed**, so that they can be adopted in the other centres and lead to a further improvement of the quality of care offered to patients with head and neck cancer. One important aspect of care where much improvement can be obtained, especially in the low-volume centres, is the **reporting of stage information to the BCR**. Knowing that assigning the proper clinical and pathological stage is one of the key activities for clinicians caring for those afflicted with cancer, it is hard to understand that for nearly one third of patients treated in lower volume centres no clinical stage information was sent to the BCR.

Another important quality of care aspect which yielded suboptimal results is the **timeliness of care**. In Denmark, they were faced with similar concerns, which were successfully resolved by organisational reforms coupled with the implementation of a fast track program.[86]
The Danish program, which was a comprehensive quality improvement project, is a perfect example of a step system where everybody plays a well-defined role, with general practitioners as the first step, private Ear, Nose and Throat (ENT) specialists as the second step and the reference centre as the third and last step. Head and neck cancer treatments are only allowed in the reference centre. Evidence that this program results in better survival was recently demonstrated.[18, 129] Also in the Netherlands, where head and neck cancer care is centralised in eight university hospitals and six affiliated centres, positive results were obtained with an integrated care program.[89]

This report is only a first step in the evaluation of care for patients afflicted by head and neck cancer in Belgium. All hospitals will receive their individual feedback report. Yet, the instalment of a **monitoring system with regular feedback to centres**, may in itself be an important leverage for quality improvement. But also, without measures it is impossible to build a picture beyond intuition.

■ RECOMMENDATIONS[I]

To the Federal Minister of Social Affairs and Public Health and the Ministers of the federated entities

- **Head and neck cancers are rare and complex cancers. To improve the quality of care and to decrease the dispersion of expertise and experience, Reference Centres should be established. These Reference Centres should have comprehensive multidisciplinary teams with recognized clinical and technical expertise in head and neck cancers, have sufficient activity that meets a minimum of quality standards, and should function within supraregional collaboration and in close collaboration with first line care. To this aim, conventions between RIZIV – INAMI and Reference Centres should be established, in line with the conventions for surgical treatment of pancreatic and oesophageal cancers.**

- **As a first step, hospitals that treat yearly 20 patients or less with a SCC of the oral cavity, oropharynx, hypopharynx or larynx (i.e. 76 Belgian hospitals in 2009-2014) should refer their patients to reference centres. All HNSCC patients have to be taken into account, without defining specific volume criteria by anatomic site. HNSCC patients with multiple tumours have to be included in the volume calculation. Similarly, patients with head and neck cancers which are even rarer (e.g. tumours of the nasal cavity and paranasal sinuses) should also be referred to reference centres.**

- **Care should be organised and coordinated in such a way that referral does not lead to a delayed start of treatment.**

- **The quality of care provided in Reference Centres should be evaluated on a regular basis, so that 'static and lifelong' certification of centres which, once recognised, can no longer demonstrate outstanding outcomes, can be avoided.**

- **Financing of the multidisciplinary oncological consultation of all cancer types should be made conditional on the compulsory and systematic registration of the cancer stage and essential predefined variables. For that purpose the BCR must transfer the status praesens of the data transfer from the reference centres on a regular basis to the RIZIV – INAMI.**

- **Access to MRI in the reference centres should be guaranteed, both for staging and follow-up of head and neck cancers.**

[I]   The KCE has sole responsibility for the recommendations.

To the National Institute for Health and Disability Insurance (RIZIV – INAMI)

- **To enable better monitoring of the quality of care for patients with head and neck cancer and to avoid that certain nomenclature codes are used for other procedures than those for which they are specified, it is important to make the nomenclature (especially for surgery) more specific and to improve invoice regulations.**

- **The list of recognised reference centres should be made easily accessible to patients (e.g. RIZIV – INAMI website).**

To the hospitals, the colleges and the scientific societies involving maxillofacial and ENT surgeons, radiation oncologists, medical oncologists, radiologists, specialists in nuclear medicine, pathologists and all healthcare providers involved in the care for head and neck cancer patients

- **Multidisciplinary teams should evaluate their individual results on the quality indicators as transmitted by the Belgian Cancer Registry, to benchmark their results and to engage into the quality improvement processes.**

- **Hospitals must properly register each cancer case and report the complete dataset including the clinical and pathological TNM stage (cTNM, pTNM, ypTNM) to the Belgian Cancer Registry.**

- **Better adherence and adoption of the invoice rules for radiotherapy (RIZIV – INAMI) are needed in order to facilitate a better interpretation of the treatment schemes.**

- **Information is needed on the inclusion of patients in clinical trials and should be transferred to the Belgian Cancer Registry.**

To the Belgian Cancer Registry

- **The following information needs to be captured/added to complete the current dataset:**

  o **P16/HPV status for oropharyngeal cancers**

  o **Type of surgical procedure (incl. purpose of procedure: diagnosis vs. treatment), organ and/or function sparing treatment**

  o **Radiotherapy schedule (e.g. fractionation scheme, start and end date)**

- o **Comorbidity, tobacco and alcohol consumption**
- **Prospective collection of patient-reported outcomes should be organised.**

To the pathological laboratories and the scientific societies of anatomopathologists

- **The pathological laboratories should provide pathological reports in synoptic and standardised format (incl. pTNM). This facilitates the collection of comprehensive and clinically relevant data (e.g. p16/HPV-status, resection margins, number of lymph nodes and localisation of positive lymph nodes).**

To the societies of radiologyand the societies involved in head and neck cancer

- **The societies should develop structured and standardised reports on the imaging of the different head and neck sites, which would facilitate the collection of relevant data for diagnosis and staging and the transfer of this information to the Belgian Cancer Registry.**

To the societies of maxillofacial and ENT surgery and the societies involved in head and neck cancer

- **The societies should develop structured and standardised surgery reports of the different head and neck sites, which would facilitate the collection of relevant data and the transfer of this information to the Belgian Cancer Registry.**

■ APPENDICES

APPENDIX 1. RARECARE DEFINITION HEAD AND NECK SQUAMOUS CELL CARCINOMA

Table 11 – Rarecare definition of head and neck squamous cell carcinoma

Type	Topography	Morphology
Oral cavity	C02.0-C02.3, C02.9, C03.0-C05.0, C06.0-C06.9	8004, 8020-8022, 8032, 8050-8076, 8078, 8082-8084, 8123, 8560
Oropharynx	C01.9, C02.4, C02.8, C05.1-C05.2, C05.8-C05.9, C09.0-C10.3, C10.8-10.9, C14.2	8004, 8020-8022, 8032, 8050-8076, 8078, 8082-8084, 8120-8121, 8123, 8560
Hypopharynx	C12.9-C13.2, C13.8-C13.9	8004, 8020-8022, 8031-8032, 8050-8076, 8078, 8082-8084, 8120, 8123, 8560
Larynx	C32.0-C32.3, C32.8-C32.9	8004, 8020-8022, 8031-8032, 8050-8076, 8078, 8082-8084, 8120, 8123, 8560

Source: http://www.rarecarenet.eu/

APPENDIX 2. IDENTIFICATION AND SELECTION OF QUALITY INDICATORS

Appendix 2.1. Medline search

Executed on 9 November 2015

1   exp Larynx/ (32071)

2   exp Oropharynx/ (12140)

3   exp Hypopharynx/ (1681)

4   exp Glottis/ (11616)

5   1 or 2 or 3 or 4 (45167)

6   exp Neoplasms/ (2794869)

7   5 and 6 (10432)

8   ((laryn* or hypopharyn* or oropharyn* or glotti* or supraglotti* or epiglotti* or subglotti*) adj5 (cancer* or tumour* or tumor* or neoplas* or malignan* or carcinoma* or metatasta*)).ti,ab. (23098)

9   exp Laryngeal Neoplasms/ (24904)

10   exp Hypopharyngeal Neoplasms/ (2569)

11   exp Oropharyngeal Neoplasms/ (6522)

12   7 or 8 or 9 or 10 or 11 (40411)

13   'Quality of Health Care'/ (61376)

14   Patient Care Management/ (2593)

15   'Organization and administration'/ (14553)

16   og.fs. (404928)

17   Quality Assurance, Health Care/ (51408)

18   Quality Indicators, Health Care/ (11637)

19   (quality adj5 (healthcare or (health adj5 care))).tw. (17704)

20   (administrative adj3 (technics or technique?)).tw. (45)

21   logistics.tw. (2916)

22   supervision.tw. (18708)

23   (quality adj3 indicator?).tw. (7522)

24   pattern$ of care.mp. (1718)

25   13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 (537951)

26   12 and 25 (108)

Appendix 2.2. Included peer-reviewed and grey publications for quality indicator identification

Table 12 – Included peer-reviewed and grey publications reporting quality indicators in the management of head and neck cancer

First author or agency	Publication year	Reference
German Cancer Society	2014	German Cancer Society. Guideline-Based Quality Indicators. 2014
Gourin	2014	Gourin CG, Frick KD, Blackford AL, Herbert RJ, Quon H, Forastiere AA, Eisele DW, Dy SM. Quality Indicators of Laryngeal Cancer Care in the Elderly. Laryngoscope 2014;124:2049–56.
Healthcare Improvement Scotland	2014	Healthcare Improvement Scotland. Head and Neck Cancer - Clinical Quality Performance Indicators. 2014.
Health and Social Care Information Centre	2014	Health and Social Care Information Centre. National Head and Neck Cancer Audit 2013. 2014.
Shellenberger	2011	Shellenberger TD, Madero-Visbal R, Weber, RS. Quality Indicators in Head and Neck Operations. A Comparison With Published Benchmarks. Arch Otolaryngol Head Neck Surg. 2011;137(11):1086-93.
Ouwens	2007	Ouwens M, Marres H, Hermens R, Hulscher M, van den Hoogen F, Grol R, Wollersheim R. Quality of integrated care for patients with head and neck cancer: development and measurement of clinical indicators. Head Neck 2007;29:378–86.

Appendix 2.3. Excluded quality indicators

Table 13 – Quality indicators excluded before actual selection phase (N=69)

Quality indicator	Source
No. of patients who are well informed on all information items.	Ouwens 2007
Availability of an information protocol.	Ouwens 2007
Staging	Gourin 2014
Pre-treatment imaging (excluding Tis or T1 glottic)	Gourin 2014
Proportion of patients with head and neck cancer who undergo CT and/or MRI of the primary site and draining lymph nodes with CT of the chest before the initiation of treatment.	Scottish Cancer Taskforce
No. of pts with oral cavity carcinoma who underwent examinations of the region from the skull base to the superior thoracic aperture with CT or MRI to determine the N stage.	German Cancer Society

Quality indicator	Source
No. of patients with stage III + IV oral cavity carcinoma who underwent chest CT to exclude pulmonary tumour involvement (metastases, second carcinoma).	German Cancer Society
Pre-treatment chest CT/CXR	National Head and Neck Cancer Audit
No. of pts with a primary diagnosis of an oral cavity carcinoma who underwent otorhinolaryngologic (ORL) examination to exclude synchronous second tumours.	German Cancer Society
No. of pts with oral cavity carcinoma who were treated with radiotherapy or chemoradiotherapy and who underwent dental examination before the start of radiotherapy or chemoradiotherapy.	German Cancer Society
Percentage of new cases of head and neck cancer confirmed as having any pre-operative/pre-treatment dental assessment.	National Head and Neck Cancer Audit
Pre-treatment dental evaluation prior to RT	Gourin 2014
Length of hospitalization 6 days	Gourin 2014
Readmission within 30 days	Gourin 2014
30 day mortality	Gourin 2014
Return to operating room within 7 days of surgery	Gourin 2014
Use of blood products.	Shellenberger 2011
Surgical site infections.	Shellenberger 2011
Proportion of patients with head and neck cancer who have extracapsular spread and/or R1 surgical margins following surgical resection who receive chemoradiation.	Scottish Cancer Taskforce
No. of pts with stages T3/T4, with close or positive resection margins, perineural or vascular invasion, or a positive lymph node who underwent postoperative radiotherapy or chemoradiotherapy.	German Cancer Society
Proportion of high-risk OPC, HPC or LC patients (e.g. close or positive resection margins, extracapsular spread) who received postoperative radiochemotherapy.	KCE Guideline
Time to start of postoperative RT 6 weeks after surgery	Gourin 2014
Proportion of patients with oropharyngeal, hypopharyngeal or laryngeal cancer in whom radiotherapy started within 6 weeks after surgery.	KCE Guideline
No. of pts with oral cavity carcinoma who were treated with radiotherapy and had no interruption of radiotherapy.	German Cancer Society
No. of patients with oral cavity carcinoma and cN0 with any T stage who underwent elective neck dissection.	German Cancer Society
No. of pts with oral cavity carcinoma who underwent surgery in whom the histological findings have been documented as follows: tumour location, macroscopic tumour size, histological tumour type according to WHO classification, histological tumour grade,	German Cancer Society

Quality indicator	Source
depth of invasion, lymphatic invasion, vascular and perineural invasion, locally infiltrated structures, pT classification, details on affected areas and infiltrated structures, R status.	
Adequacy of pathology reports.	Shellenberger 2011
Hospice care>7 days before death from cancer	Gourin 2014
No chemotherapy within 14 days of death from cancer	Gourin 2014
Death from cancer not in acute setting	Gourin 2014
No ICU care in last 30 days of life	Gourin 2014
No acute care in last 30 days of life	Gourin 2014
Proportion of patients with a resectable locoregional recurrence in spite of previous radiotherapy or surgery, in whom salvage surgery was performed by a dedicated surgical team with adequate experience in reconstructive techniques in a centre that offers suitable intensive care support.	KCE Guideline
Proportion of patients with a non-resectable locoregional recurrence in spite of previous irradiation, who underwent re-irradiation in a facility with adequate expertise (ideally as part of a clinical study).	KCE Guideline
Appropriate surgery (no surgery for distant metastatic disease)	Gourin 2014
Appropriate radiation (if no previous RT)	Gourin 2014
Appropriate chemotherapy	Gourin 2014
Hospice for distant metastatic disease not treated with chemotherapy	Gourin 2014
Time to start of postoperative RT 6 weeks after surgery	Gourin 2014
Follow-up according to specified protocol	Gourin 2014
Dental evaluation if received RT	Gourin 2014
No. of patients with swallowing problems after leaving the hospital who were offered arrangements about follow-up.	Ouwens 2007
Pre-treatment speech and language therapy (SALT) assessment	National Head and Neck Cancer Audit
Proportion of patients with oral, pharyngeal or laryngeal cancer who are seen by a Specialist SLT before treatment.	Scottish Cancer Taskforce
No. of patients who had a radical neck dissection or radiation in this area and with whom arrangements were made about follow-up regarding their speech revalidation.	Ouwens 2007
Proportion of patients with head and neck cancer who undergo nutritional screening with the Malnutrition Universal Screening Tool (MUST) before first treatment.	Scottish Cancer Taskforce

Quality indicator	Source
Percentage of new cases of head and neck cancer confirmed as having any pre-operative/pre-treatment (includes radio and chemotherapy) dietetic assessment.	National Head and Neck Cancer Audit
No. of patients who were monitored regarding their nutrition health status before, during, and after their treatment.	Ouwens 2007
No. of patients who were informed about the possibilities to contact companions in distress.	Ouwens 2007
No. of patients who said they were offered emotional support.	Ouwens 2007
No. of patients with oral cavity carcinoma who received interdisciplinary treatment following vote on tumour board including the specialties of oral and maxillofacial surgery, ORL, radiotherapy, oncology, pathology and radiology.	German Cancer Society
Percentage of new cases of head and neck cancer discussed at MDT.	National Head and Neck Cancer Audit
Percentage of new cases of head and neck cancer where confirmed as seen by a Clinical Nurse Specialist (CNS) prior to commencement of treatment.	National Head and Neck Cancer Audit
No. of patients who were informed about the possibilities to contact companions in distress.	Ouwens 2007
30 day mortality	Gourin 2014
Proportion of patients with head and neck cancer who smoke who are referred to smoking cessation before first treatment.	Scottish Cancer Taskforce
Availability of a multidisciplinary stop-smoking protocol.	Ouwens 2007
No. of patients who had been asked about smoking behaviour.	Ouwens 2007
No. of smokers who were offered support to stop smoking.	Ouwens 2007
Availability of a multidisciplinary alcohol abstinence protocol.	Ouwens 2007
No. of patients who had been asked about alcohol use.	Ouwens 2007
No. of patients with alcohol problems who were offered support.	Ouwens 2007
Functioning of the multidisciplinary patient care team according to the team climate inventory.	Ouwens 2007
Availability of an integrated care pathway for patients with head and neck cancer.	Ouwens 2007
The use of the clinical pathway for each patient with head and neck cancer.	Ouwens 2007
Availability of a case manager.	Ouwens 2007
The no. of patients that had interaction with the case manager(s).	Ouwens 2007
No. of patients who said that transition went seamlessly: to the head and neck centre, within the hospital between departments, from the head and neck centre returning home.	Ouwens 2007
Proportion of patients in whom treatment started within three weeks.	Added by expert

Appendix 2.4.   Quality indicator evaluation on relevance

Table 14 – Quality indicator evaluation on relevance

Score	Selection based on relevance
≥ 70%	58
50-70%	23
< 50%	26

Table 15 – Quality indicators excluded after 1st selection phase (N=49)

Quality indicator	Source	Min. score	Max. score	Median score	Mean score	% 4-5 score
Proportion of patients with head and neck cancer (by localisation) who underwent p16 testing.	KCE Guideline	3	5	4	3.9	67%
Proportion of new cases of head and neck cancer where the interval from biopsy to reporting is less than ten days.	National Head and Neck Cancer Audit	3	5	4	3.8	67%
Proportion of patients with oropharyngeal, hypopharyngeal or laryngeal cancer who were treated with concurrent postoperative chemoradiotherapy, in whom radiotherapy was fractionated conventionally (i.e. 2 Gy per fraction, 5 days per week, total dose 64-66 Gy) and chemotherapy was platinum-based (100 mg/m² 3-weekly).	KCE Guideline	1	5	4	3.8	67%
Proportion of patients with head and neck cancer treated with surgery, in whom intraoperative frozen sections were taken.	KCE Guideline	1	5	4	3.3	67%
Proportion of patients with head and neck cancer who received follow-up at least every three months in the first and second year, six months in the third to fifth year, and annually afterwards.	KCE Guideline	2	5	4	3.9	64%
Proportion of patients having undergone surgery and/or irradiation for carcinoma of the oral cavity, who attend regular dental check-ups.	KCE Guideline	2	5	4	3.5	64%
Proportion of patients who know who to talk to for information and questions.	Ouwens 2007	1	5	4	3.5	64%

Quality indicator	Source	Min. score	Max. score	Median score	Mean score	% 4-5 score
Frequency of MTD meetings.	Added by expert	2	5	4	3.9	60%
Proportion of patients with oral cavity cancer and a microscopically residual tumour (R1 resection) who underwent targeted follow-up resection.	KCE Guideline	3	5	4	3.8	60%
Proportion of patients with stage II oropharyngeal, hypopharyngeal or laryngeal cancer who received primary radiotherapy with altered fractionation (hyperfractionation or accelerated fractionation without dose reduction).	KCE Guideline	1	5	4	3.7	60%
Proportion of patients with head and neck cancer in whom a distance of at least 10 mm from the palpable tumour margin is observed during resection.	KCE Guideline	1	5	4	3.4	60%
Proportion of patients with metastatic head and neck cancer or recurrent disease that is not eligible for curative treatment, who received palliative chemotherapy or targeted treatment.	KCE Guideline	1	4	4	3.2	60%
Proportion of patients with head and neck SCC whose pathology specimens have been sent for revision to the reference laboratory for diagnosis confirmation upon request from the reference centre, after referral to another centre/reference centre (for work-up completion and treatment) and approval that no additional biopsies are needed.	KCE Guideline	3	5	4	3.7	58%
Proportion of patients with non-metastatic oral cavity cancer that is at or crossing the midline or not clearly localized laterally, who received a contralateral neck dissection.	KCE Guideline	2	5	4	3.7	55%
Proportion of patients with non-small, non-lateralised oropharyngeal, hypopharyngeal or supraglottic cancer who received bilateral selective neck treatment.	KCE Guideline	1	5	4	3.6	55%
Proportion of patients with oral cavity cancer who underwent surgical resection and immediate reconstruction.	KCE Guideline	1	5	4	3.5	55%

Quality indicator	Source	Min. score	Max. score	Median score	Mean score	% 4-5 score
Proportion of patients with early (stage I or II) glottic cancer without supraglottic extension who did not receive neck treatment.	KCE Guideline	1	5	4	3.5	55%
Proportion of patients with advanced and non-metastatic oral cavity carcinoma who were not eligible for curative surgery (T4b, N3, unacceptable functional consequences, excessive comorbidity), who received (1) primary radiochemotherapy or (2) radiotherapy alone.	KCE Guideline	1	5	4	3.5	55%
Proportion of patients with small lateralised oropharyngeal, hypopharyngeal and supraglottic cancer who received unilateral neck treatment.	KCE Guideline	1	5	4	3.5	55%
Proportion of patients who feel involved in decisions regarding their treatment.	Ouwens 2007	1	5	3,5	3.1	55%
Proportion of pts with head and neck cancer and with documented offer of psychosocial care provided by a social worker.	German Cancer Society	2	5	3,25	3.7	50%
Proportion of patients with locally-advanced oropharyngeal, hypopharyngeal or laryngeal cancer in whom a non-surgical approach is chosen and in whom concomitant chemoradiotherapy is not an option, who received primary radiotherapy with hyperfractionation or accelerated fractionation without dose reduction.	KCE Guideline	1	5	3,5	3.3	50%
Proportion of patients with head and neck cancer who received primary radiotherapy with accelerated fractionation with dose reduction.	KCE Guideline	1	5	3,5	3.2	50%
Proportion of patients with oral cavity cancer who did not receive induction chemotherapy.	KCE Guideline	1	5	3	3.1	45%
Proportion of patients with head and neck cancer who received TSH screening after RT	Gourin 2014	1	5	3	3.3	44%
Proportion of patients with oral cavity cancer and no radiological or intraoperative evidence of tumour invasion of the bone in whom the continuity of the mandible was preserved.	KCE Guideline	1	4	3	3.1	44%

Quality indicator	Source	Min. score	Max. score	Median score	Mean score	% 4-5 score
Proportion of patients with head and neck cancer who were treated with postoperative radiotherapy in whom the radiotherapy was fractionated conventionally (e.g. 60-66 Gy in 6 to 6.5 weeks, 2 Gy per day, 5 times a week).	KCE Guideline	1	5	3	3.6	40%
Proportion of patients with head and neck cancer evaluated by multidisciplinary team (incl anesthesiologist / ICU doc / nutritionist / speech therapist).	Added by expert	2	4	3	3.2	40%
Proportion of patients with head and neck cancer who were treated with radiotherapy of the head and neck region and who received lifelong extra fluoride applications.	KCE Guideline	1	5	3	3.1	40%
Proportion of patients who started their first treatment within xxx days after their first visit to the specialist.	Ouwens 2007	1	4	3	3.1	40%
Proportion of patients with head and neck cancer undergoing surgery with a return to the operating room within 7 days of the operation.	Shellenberger 2011	3	5	3	3.5	36%
Proportion of patients with locally-advanced hypopharyngeal or laryngeal cancer who received induction chemotherapy.	KCE Guideline	1	5	3	3.1	36%
Proportion of patients with oropharyngeal cancer who did not receive induction chemotherapy.	KCE Guideline	1	5	3	3.0	36%
Proportion of patients with head and neck cancer undergoing surgery with a wound infection within 30 days of surgery.	Gourin 2014	1	5	3	3.2	30%
Proportion of patients with suspected recurrence in the head and neck region that could not be confirmed or ruled out by CT and/or MRI, who underwent FDG-PET(/CT) .	KCE Guideline	1	5	3	3.1	30%
Proportion of patients with head and neck cancer who received posttreatment imaging (if T3/4 or N2/3)	Gourin 2014	1	5	2.5	2.8	30%
Proportion of patients with head and neck cancer who received appropriate chemotherapy.	Gourin 2014	1	5	3	2.9	27%

Quality indicator	Source	Min. score	Max. score	Median score	Mean score	% 4-5 score
Proportion of patients with oral cavity cancer who did not receive the combination of radiotherapy with EGFR inhibitors.	KCE Guideline	1	5	3	2.8	27%
Proportion of patients with head and neck cancer in whom induction chemotherapy was given within the context of a function-sparing strategy.	KCE Guideline	1	5	3	2.7	27%
Proportion of patients who could see a specialist 1 day after referral.	Ouwens 2007	1	4	2	2.5	27%
Proportion of patients with head and neck cancer undergoing surgery with a readmission within 30 days of the operation.	Shellenberger 2011	1	5	3	3.0	18%
Proportion of patients with head and neck cancer who were hospitalised within 30 days of treatment.	Gourin 2014	1	4	2	2.5	18%
Proportion of patients with head and neck cancer undergoing surgery with a length of stay at ICU of at least xxx days.	Added by expert	1	4	3	2.6	14%
Proportion of patients with head and neck cancer who received airway protective tracheostomy.	Added by expert	1	4	2	2.4	14%
Proportion of patients with head and neck cancer who were admitted to ICU.	Added by expert	1	4	3	2.8	13%
Proportion of patients with head and neck cancer undergoing surgery with a length of stay of at least xxx days.	Shellenberger 2011	1	5	3	2.8	11%
Proportion of patients with head and neck cancer undergoing surgery who received a blood transfusion.	Gourin 2014	1	4	3	2.6	11%
Proportion of patients with small but accessible tumours (T1/T2) in the oral cavity (e.g. lips) who were treated with interstitial brachytherapy.	KCE Guideline	1	4	2	2.1	10%
Proportion of patients who had all necessary diagnostic procedures on day of their first visit to the specialist.	Ouwens 2007	1	4	2	2.3	9%

Table 16 – Quality indicators excluded after 2nd selection phase (N=12)

Quality indicator	Source	Min. score	Max. score	Median score	Mean score	% 4-5 score
Proportion of patients with an uncommon tumour diagnosis (i.e. non-SCC) whose pathology specimens/diagnosis are/is reviewed by an expert from a reference laboratory, after referral to another centre/reference centre.	KCE Guideline	3	5	4	4.3	92%
Proportion of patients with head and neck cancer undergoing radiotherapy who received IMRT.	Scottish Cancer Taskforce	3	5	5	4.6	91%
Proportion of patients with head and neck cancer in whom management of the lymph nodes followed the same treatment principles as those applied for the primary tumour.	KCE Guideline	3	5	4	4.3	91%
Proportion of patients with head and neck cancer undergoing appropriate surgery (neck dissection if indicated based on stage or site with primary ablative surgery for N0 disease if not followed by postoperative radiation, or for N1 disease if primary ablative surgery performed; no surgery for T4b disease)	Gourin 2014	3	5	5	4.5	88%
Proportion of patients with head and neck cancer with a histologic confirmation of disease.	Gourin 2014	2	5	5	4.4	83%
Proportion of patients with HNSCC and (infected) osteoradionecrosis of the jaw.	KCE Guideline	2	5	5	4.2	82%
Proportion of patients with head and neck cancer who received chemoradiotherapy at a facility in which radiotherapy- or chemotherapy-induced acute toxicities can be adequately managed.	KCE Guideline	1	5	5	4.2	73%
Proportion of patients with a resectable locoregional recurrence in spite of primary treatment with curative intent, in whom salvage surgery is performed by an experienced surgical team.	KCE Guideline	1	5	4	3.6	73%
Proportion of patients who are well informed on all information items applicable to their situation.	Ouwens 2007	1	5	4	3.8	73%
Proportion of patients with head and neck cancer undergoing appropriate radiation.	Gourin 2014	1	5	4	3.8	70%
Number of dedicated physicians.	Added by expert	2	5	5	4.1	70%
Proportion of patients with a time window between first call and 1st appointment of maximum 14 days.	Added by expert	2	5	4	3.9	70%

Table 17 – Quality indicators merged with one of the included indicators (N=14)

Quality indicator	Source	Min. score	Max. score	Median score	Mean score	% 4-5 score
Proportion of patients having eating and speaking problems due to carcinoma of the oral cavity and/or its management who have had a consultation with a dedicated nutritional therapist before, during and after treatment.	KCE Guideline	3	5	5	4.5	91%
Proportion of patients with dysphagia who underwent appropriate diagnostic procedures, e.g. clinical exam by the speech therapist, videofluoroscopy or fiber-optic endoscopy.	KCE Guideline	3	5	4	4.4	91%
Proportion of patients having eating and speaking problems due to carcinoma of the oral cavity and/or its management who have had a consultation with a dedicated speech therapist before, during and after treatment.	KCE Guideline	3	5	4	4.4	91%
Proportion of patients with head and neck cancer at risk for malnutrition who received dietary counselling and nutritional therapy.	KCE Guideline	2	5	5	4.4	91%
Proportion of patients with head and neck cancer who are screened for malnutrition.	KCE Guideline	2	5	4	4.3	91%
Proportion of patients with HNSCC who were introduced to suitably qualified therapists prior to commencing treatment if the scheduled surgical or conservative procedures (e.g. radiotherapy) were likely to cause problems with chewing, swallowing and/or speech.	KCE Guideline	2	5	4	4.2	90%
Proportion of patients with head and neck cancer of whom resective pathology was discussed at MDT.	National Head and Neck Cancer Audit	3	5	5	4.4	73%
Proportion of patients with head and neck cancer who are discussed at a MDT before definitive treatment.	Scottish Cancer Taskforce	3	5	5	4.7	91%
30-day mortality after surgery.	Shellenberger 2011	1	5	4	3.8	73%
Proportion of patients with advanced pT categories (T3/T4) OPC, HPC or LC with lymph node involvement (> pN1), perineural extension or lymphatic vessel infiltration who received postoperative radiotherapy.	KCE Guideline	3	5	5	4.4	73%

Quality indicator	Source	Min. score	Max. score	Median score	Mean score	% 4-5 score
Proportion of patients with oral cavity cancer who were treated with postoperative radiotherapy in whom the radiotherapy was completed within 12-13 weeks after surgery.	KCE Guideline	3	5	4,5	4.3	80%
Proportion of patients with oropharyngeal, hypopharyngeal or laryngeal cancer in whom radiotherapy was completed within 11-13 weeks after surgery.	KCE Guideline	3	5	4	4.2	78%
Proportion of patients with oral cavity cancer who were treated with primary (chemo)radiotherapy who underwent diagnostic evaluation of the neck with conventional imaging techniques (CT or MRI) or PET(/CT) three months after completion of primary (chemo)radiotherapy.	KCE Guideline	2	5	4	4.0	73%
Proportion of patients with oropharyngeal, hypopharyngeal or laryngeal cancer (N1-3) and complete response to chemoradiotherapy (assessed by FDG-PET(/CT) or DW-MRI), who did not receive an additional lymph node dissection.	KCE Guideline	3	5	4	4.0	73%

Table 18 – Quality indicators that are not measurable with administrative data (N=18)

Quality indicator	Source	Reason(s) for not being measurable
Proportion of biopsy reports that include: tumour localization, tumour histology, tumour grade, depth of invasion (if assessable), lymphatic, vascular and perineural invasion.	KCE Guideline	Clinical information not available in BCR database
Proportion of patients with head and neck cancer who underwent clinical examination (including fiberoptic examination) of the upper aerodigestive tract.	KCE Guideline	Nomenclature codes do not allow judgement of the content of a consultation
Proportion of patients with head and neck cancer treated with radiotherapy in whom radiotherapy was not interrupted.	KCE Guideline	Interruption of radiotherapy is not captured by nomenclature codes
Proportion of patients with head and neck cancer who underwent surgical resection with curative intent where R0 resection was achieved.	Scottish Cancer Taskforce	Clinical information, such as R-status, is not recorded by BCR or captured by nomenclature codes
Availability of a multidisciplinary patient care team.	Ouwens 2007	Is not recorded with administrative data

Quality indicator	Source	Reason(s) for not being measurable
Proportion of patients with head and neck cancer who underwent surgery in whom the histological findings have been documented as follows: tumour localization, macroscopic tumour size, histological tumour type, histological tumour grade, depth of invasion, lymphatic, vascular and perineural invasion, locally infiltrated structures, pT classification, details of affected areas and infiltrated structures, R status and p16 (if not done on biopsy).	KCE Guideline	Clinical information not available in BCR database
Proportion of patients with head and neck cancer treated with neck dissection in whom the pathology report contains the following information: anatomical topography, the side of the neck, type of neck dissection, eliminated levels, total number of lymph nodes plus number of lymph nodes affected, number of lymph nodes per level, level of the affected lymph nodes, diameter of the largest tumour deposit, additionally removed structures and, if present, extracapsular spread.	KCE Guideline	Clinical information not available in BCR database
Proportion of non-edentulous patients with head and neck cancer who have had an oral examination before initiation of treatment.	Scottish Cancer Taskforce	Clinical information, such as dentate status, is not recorded by BCR or captured by nomenclature codes
Proportion of patients with advanced pT categories (T3/T4) head and neck cancer, close (< 4 mm) or positive resection margins, tumour thickness > 10 mm, lymph node involvement (> pN1), extra capsular rupture/soft tissue infiltration, perineural extension or lymphatic vessels infiltration who received postoperative radiotherapy.	KCE Guideline	Clinical information not available in BCR database
Proportion of patients with chewing, speaking and swallowing problems after HNSCC treatment, who were timely provided with appropriate functional therapy.	KCE Guideline	Clinical information (e.g. chewing, speaking and swallowing problems) not available in BCR database
Proportion of high-risk patients (e.g. close or positive resection margins, extracapsular spread) who received postoperative radiochemotherapy.	KCE Guideline	Clinical information (e.g. close or positive resection margins, extracapsular spread) not available in BCR database
Proportion of patients with oral cavity cancer (N1-3) and complete response to chemoradiotherapy (assessed by FDG-PET(/CT) , CT or MRI), who did not receive an additional lymph node dissection.	KCE Guideline	Clinical information (e.g. response to treatment) not available in BCR database
Proportion of patients with a non-resectable locoregional recurrence after primary treatment with curative intent, who underwent re-irradiation.	KCE Guideline	Recurrence not recorded by BCR as a new event
Proportion of patients with cN+M0 oral cavity cancer who were treated surgically and who underwent a selective ipsilateral neck dissection of at least level I, II, III and IV with – if oncologically feasible – preservation of the sternocleidomastoid muscle, jugular vein and spinal accessory nerve.	KCE Guideline	Too detailed information on surgical intervention, not captured by nomenclature codes

Quality indicator	Source	Reason(s) for not being measurable
Proportion of patients with head and neck cancer who received concurrent (primary or postoperative) radiochemotherapy, in whom a cumulative dose of 200 mg/m² was given.	KCE Guideline	Dosage of chemotherapy not captured by administrative codes
Nasogastric tube or gastrostomy tube feeding proportions before, just after treatment and at 1 year (+ time length of tube dependency).	Added by expert	No specific codes for tube feeding
Proportion of patients with metastatic or recurrent HNSCC being included in a clinical trial.	Added by expert	Inclusion in clinical trial is not recorded in administrative databases used
Proportion of patients with advanced oropharyngeal, hypopharyngeal or laryngeal cancer who underwent an organ- and/or function-sparing procedure	KCE Guideline	Impossible to identify organ- and/or function sparing procedures in the used administrative databases

Table 19 – Quality indicators excluded in the final round (N=2)

Quality indicator	Source	Reason for exclusion
Proportion of patients with HNSCC who have a cytological or histological diagnosis before treatment.	Scottish Cancer Taskforce	Clinical information not available in BCR database
Proportion of patients with head and neck cancer who underwent clinical examination (including fiberoptic examination) of the upper aerodigestive tract.	KCE Guideline	Nomenclature codes do not allow judgement of the content of a consultation

APPENDIX 3. BILLING CODES

Appendix 3.1. Nomenclature codes for diagnostic procedures

Appendix 3.1.1. Codes for multidisciplinary team meeting (MDT)

Table 20 – Nomenclature codes multidisciplinary team meeting (MDT)

Outpatient	Inpatient	Dutch Description	French Description
350276	350280	01/11/2010: Opvolgings-multidisciplinair oncologisch consult (opvolgings-MOC), geattesteerd door de geneesheer-coördinator	01/11/2010 : Concertation oncologique multidisciplinaire de suivi (COM de suivi), attestée par le médecin-coordinateur
350291	350302	01/11/2010: Bijkomend multidisciplinair oncologisch consult (bijkomende MOC) in een ander ziekenhuis dan dit van het eerste MOC, op doorverwijzing, geattesteerd door de geneesheer-coördinator	01/11/2010 : Concertation oncologique multidisciplinaire supplémentaire (COM supplémentaire) dans un hôpital autre que celui de la première COM, sur renvoi, attestée par le médecin-coordinateur
350372	350383	01/11/2010: Eerste multidisciplinair oncologisch consult (eerste MOC), geattesteerd door de geneesheer-coördinator	01/11/2010 : Première consultation oncologique multidisciplinaire (première COM), attestée par le médecin-coordinateur
		01/02/2003: Schriftelijk verslag van een multidisciplinair oncologisch consult met deelname van minstens drie geneesheren van verschillende specialismen onder leiding van een geneesheer-coördinator, met beschrijving van de diagnose en van het behandelingsplan	01/02/2003 : Rapport écrit d'une concertation oncologique multidisciplinaire avec la participation d'au moins trois médecins de spécialités différentes sous la direction d'un médecin-coordinateur et reprenant la description du diagnostic et du plan de traitement
350394	350405	Deelname aan multidisciplinair oncologisch consult	Participation à la concertation oncologique multidisciplinaire
350416	350420	01/11/2010: Deelname aan het multidisciplinair oncologisch consult door een arts die geen deel uitmaakt van de staf van ziekenhuisgeneesheren	01/11/2010 : Participation à la concertation oncologique multidisciplinaire par un médecin qui n'est pas membre de l'équipe de médecins hospitaliers
		01/02/2003: Deelname aan multidisciplinair oncologisch consult door de behandelende arts die geen deel uitmaakt van de ziekenhuisstaf	01/02/2003 : Participation à la concertation oncologique multidisciplinaire par le médecin traitant qui n'est pas membre de l'équipe hospitalière
350453	350464	01/11/2010: Bijkomend honorarium bij de verstrekking 350372-350383, 350276-350280 en 350291-350302 aanrekenbaar door de geneesheer-specialist in de medische oncologie, of houder van de bijzondere beroepstitel in de klinische hematologie of in de pediatrische hematologie en oncologie, wanneer deze het multidisciplinair oncologisch consult coördineert	01/11/2010 : Supplément d'honoraires à la prestation 350372-350383, 350276-350280 et 350291-350302, attestable par le médecin spécialiste en oncologie médicale ou porteur du titre professionnel particulier en hématologie clinique ou en hématologie et oncologie pédiatriques, lorsque celui-ci coordonne la consultation oncologique multidisciplinaire
		01/03/2010: Bijkomend honorarium bij de verstrekking 350372-350383 aanrekenbaar door de geneesheer-specialist in de medische oncologie,	01/03/2010 : Supplément d'honoraires à la prestation 350372-350383, attestable par le médecin spécialiste en oncologie médicale ou porteur

Outpatient	Inpatient	Dutch Description	French Description
		of houder van de bijzondere beroepstitel in de klinische hematologie of in de pediatrische hematologie en oncologie, wanneer deze het multidisciplinair oncologisch consult coördineert	du titre professionnel particulier en hématologie clinique ou en hématologie et oncologie pédiatriques, lorsque celui-ci coordonne la consultation oncologique multidisciplinaire
350475	350486	01/03/2010: Bijkomend honorarium bij de verstrekking 350394-350405 of 350416-350420 aanrekenbaar door de geneesheer-specialist in de medische oncologie, of houder van de bijzondere beroepstitel in de klinische hematologie of in de pediatrische hematologie en oncologie, wanneer deze het multidisciplinair oncologisch consult bijwoont	01/03/2010 : Supplément d'honoraires à la prestation 350394-350405 ou 350416-350420, attestable par le médecin spécialiste en oncologie médicale ou porteur du titre professionnel particulier en hématologie clinique ou en hématologie et oncologie pédiatriques, lorsque celui-ci assiste à la consultation oncologique multidisciplinaire

Appendix 3.1.2. Codes for imaging

Table 21 – Nomenclature codes RX thorax

Outpatient	Inpatient	Dutch Description	French Description
452690	452701	Radiografie van de thorax en de inhoud ervan, één cliché	Radiographie du thorax et de son contenu, un cliché
452712	452723	Radiografie van de thorax en de inhoud ervan, minimum 2 clichés	Radiographie du thorax et de son contenu, minimum 2 clichés
463691	463702	Radiografie van de thorax en de inhoud ervan, één cliché	Radiographie du thorax et de son contenu, un cliché
463713	463724	Radiografie van de thorax en de inhoud ervan, minimum 2 clichés	Radiographie du thorax et de son contenu, minimum 2 clichés
455335*	455346*	Radiografie van het ribrooster, minimum twee clichés	Radiographie du gril costal, minimum 2 clichés

This nomenclature code is added to the selection because it cannot be billed on the same day as the regular RX thorax codes and has a higher key value.

Table 22 – Nomenclature codes RX swallow mechanism/oesophagus

Outpatient	Inpatient	Dutch Description	French Description
451076	451080	Radiografie van het slikmechanisme farynx-hypofarynx, met radioscopisch onderzoek met beeldversterker en televisie in gesloten keten, minimum zes clichés	Radiographie du mécanisme de déglutition pharynx-hypopharynx, avec examen radioscopique avec amplificateur de brillance et chaîne de télévision, minimum 6 clichés
451091	451102	Bijkomend honorarium ingeval verstrekking nr. 451076 - 451080 wordt aangevuld met magnetisch registreren van de beelden	Supplément au cas où la prestation 451076 - 451080 est complétée par un enregistrement magnétique des images
451135	451146	Radiografie van de oesofagus met radioscopisch onderzoek met beeldversterker en televisie in gesloten keten, minimum zes clichés	Radiographie de l'œsophage avec examen radioscopique avec amplificateur de brillance et chaîne de télévision, minimum 6 clichés

Table 23 – Nomenclature codes RX larynx

Outpatient	Inpatient	Dutch Description	French Description
452793	452804	Radiografie van de larynx, eventueel met de trachea, zonder contrastmiddel, minimum twee clichés	Radiographie du larynx, avec trachée éventuellement, sans préparation opaque, minimum 2 clichés
463794	463805	Radiografie van de larynx, eventueel met de trachea, zonder contrastmiddel, minimum twee clichés	Radiographie du larynx, avec trachée éventuellement, sans préparation opaque, minimum 2 clichés

Table 24 – Nomenclature codes CT neck

Outpatient	Inpatient	Dutch Description	French Description
458813	458824	01/11/1992: Computergestuurde tomografie van de hals (weke delen) of van de thorax of van het abdomen, met en/of zonder contrastmiddel, met registreren en clichés, minimum 15 coupes, voor het hele onderzoek	01/11/1992 : Tomographie commandée par ordinateur, du cou (parties molles) ou du thorax, ou de l'abdomen, avec et/ou sans moyen de contraste, avec enregistrement et clichés, 15 coupes au minimum, pour l'ensemble de l'examen
		01/10/2010: Computergestuurde tomografie van de hals (weke delen) met of zonder contrastmiddel, met registreren en clichés, minimum 15 coupes, voor het hele onderzoek	01/10/2010 : Tomographie commandée par ordinateur, du cou (parties molles) avec/ou sans moyen de contraste, avec enregistrement et clichés, 15 coupes au minimum, pour l'ensemble de l'examen
459594	459605	01/10/2010: Computergestuurde tomografie van de hals en de thorax, met of zonder contrastmiddel, met registreren en clichés, minimum 30 coupes voor het hele onderzoek	Tomographie commandée par ordinateur du cou et du thorax, avec/ ou sans moyen de contraste, avec enregistrement et clichés, 30 coupes au minimum, pour l'ensemble de l'examen
459631	459642	01/10/2010: Computergestuurde tomografie van de hals, de thorax en het abdomen, met of zonder contrastmiddel, met registreren en clichés, minimum 30 coupes voor het hele onderzoek	01/10/2010 : Tomographie commandée par ordinateur du cou, du thorax et de l'abdomen, avec/ou sans moyen de contraste, avec enregistrement et clichés, 30 coupes au minimum, pour l'ensemble de l'examen

Table 25 – Nomenclature codes CT skull

Outpatient	Inpatient	Dutch Description	French Description
458673	458684	01/11/1992: Computergestuurde tomografie van de schedel en/of van faciaal massief, met en/of zonder contrastmiddel, met registreren en clichés, minimum 10 coupes, voor het hele onderzoek	01/11/1992 : Tomographie du crâne et/ou du massif facial, commandée par ordinateur, avec et/ou sans moyen de contraste, avec enregistrement et clichés, 10 coupes au minimum pour l'ensemble de l'examen
		01/02/2012: Computergestuurde tomografie van de schedel met en/of zonder contrastmiddel, met registreren en clichés, minimum 10 coupes, voor het hele onderzoek	01/02/2012 : Tomographie du crâne commandée par ordinateur, avec et/ou sans moyen de contraste, avec enregistrement et clichés, 10 coupes au minimum pour l'ensemble de l'examen

Outpatient	Inpatient	Dutch Description	French Description
		05/05/2016: Computergestuurde tomografie van de schedel met of zonder contrast, met registreren en clichés, minimum 10 coupes, voor het hele onderzoek	05/05/2016 : Tomographie du crâne commandée par ordinateur, avec ou sans moyen de contraste, avec enregistrement et clichés, 10 coupes au minimum pour l'ensemble de l'examen

Table 26 – Nomenclature codes MRI neck

Outpatient	Inpatient	Dutch Description	French Description
459410	459421	NMR-onderzoek van de hals of van de thorax of van het abdomen of van het bekken, minstens drie sequenties, met of zonder contrast, met registratie op optische of elektromagnetische drager	Examen d'IRM du cou ou du thorax ou de l'abdomen ou du bassin, minimum 3 séquences, avec ou sans contraste, avec enregistrement sur support soit optique, soit électromagnétique

Table 27 – Nomenclature codes MRI head*

Outpatient	Inpatient	Dutch Description	French Description
459395	459406	NMR-onderzoek van het hoofd (schedel, hersenen, rotsbeen, hypofyse, sinussen,orbita(e) of kaakgewrichten), minstens drie sequenties, met of zonder contrast, met registratie op optische of elektromagnetische drager	Examen d'IRM de la tête (crâne, encéphale, rocher, hypophyse, sinus, orbite(s) ou articulations de la mâchoire), minimum 3 séquences avec ou sans contraste, avec enregistrement soit sur support optique, soit électromagnétique

* In the analyses, the nomenclature code for MRI head is also used for an MRI of the primary tumour for oral cavity and oropharynx tumours.

Table 28 – Nomenclature codes PET(/CT)

Outpatient	Inpatient	Dutch Description	French Description
442971	442982	01/07/1999: Positronentomografisch onderzoek door coïncidentiedetectie met protocol en documenten, voor het geheel van het onderzoek	01/07/1999 : Tomographie à positrons par détection en coïncidence avec protocole et documents, pour l'ensemble de l'examen
		01/01/2016: Positronentomografisch onderzoek door coïncidentiedetectie met protocol en documenten, voor het geheel van het onderzoek, voor oncologische indicaties	01/01/2016 : Tomographie à émission de positons par détection en coïncidence avec protocole et documents, pour l'ensemble de l'examen, pour des indications oncologiques
442595	442606	01/11/1998 – 31/12/2015: Functionele scintigrafische test die twee opeenvolgende tomografische onderzoeken omvat, met verwerking op computer, die tenminste twee niet-parallelle reconstructievlakken omvat, met protocol en iconografische documenten, niet cumuleerbaar met de verstrekkingen 442411 - 442422, 442455 - 442466, 442610 - 442621 en	01/11/1998 – 31/12/2015: Test scintigraphique fonctionnel comportant deux examens tomographiques successifs avec traitement par ordinateur comprenant au moins deux plans non parallèles de reconstruction, avec protocole et documents iconographiques, non cumulable avec les prestations 442411 - 442422, 442455 - 442466,

Outpatient	Inpatient	Dutch Description	French Description
		442632 - 442643 voor het onderzoek van een zelfde functie dat met een zelfde gemerkt produkt wordt verricht	442610 - 442621 et 442632 - 442643 pour l'examen d'une même fonction effectué au moyen d'un même produit marqué

Table 29 – Nomenclature codes ultrasound neck

Outpatient	Inpatient	Dutch Description	French Description
460095	460106	1/11/1994: Echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens, ongeacht het aantal echogrammen: Van de hals	01/11/1994 : Echographie avec protocole écrit et support iconographique issu d'un traitement digital des données, quel que soit le nombre d'échogrammes : Du cou
		1/04/2003: Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens, ongeacht het aantal echogrammen: Van de hals	01/04/2003 : Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données, quel que soit le nombre d'échogrammes : Du cou
469350	469361	Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens ongeacht het aantal echogrammen: Van de hals	Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données quel que soit le nombre d'échogrammes : Du cou

Table 30 – Nomenclature codes ultrasound abdomen

Outpatient	Inpatient	Dutch Description	French Description
459712	459723	Totaal abdominaal onderzoek (lever, galblaas, milt, pancreas, nieren of bijnieren, retroperitoneum) waarbij minstens acht verschillende sneden gedokumenteerd inclusief eventueel gebruik van dopplertechnieken	Examen abdominal total (foie, vésicule biliaire, rate, pancréas, reins ou surrénales, rétropéritoine) avec au minimum huit coupes différentes documentées, y compris l'usage éventuel de techniques doppler
460154	460165	Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens, ongeacht het aantal echogrammen: Van het abdomen: Lever en/of galblaas, en/of galwegen	Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données, quel que soit le nombre d'échogrammes : De l'abdomen : Le foie et/ou la vésicule biliaire et/ou les voies biliaires
469416	469420	Bidimensionele echografie met geschreven protocol en iconografische drager die ontstaat na digitale beeldverwerking van de gegevens ongeacht het aantal echogrammen - Van het abdomen: Lever en/of galblaas en/of galwegen	Echographie bidimensionnelle avec protocole écrit et support iconographique issu d'un traitement digital des données quel que soit le nombre d'échogrammes - De l'abdomen : Le foie et/ou la vésicule biliaire et/ou les voies biliaires
469173	469184	01/03/2010: Totaal abdominaal onderzoek (lever, galblaas, milt, pancreas, nieren of bijnieren, retroperitoneum) waarbij minstens acht verschillende sneden gedokumenteerd	01/03/2010: Examen abdominal total (foie, vésicule biliaire, rate, pancréas, reins ou glandes surrénales, rétropéritoine) avec au moins huit coupes documentées différentes

Appendix 3.1.3. Codes for endoscopy

Table 31 – Nomenclature codes tracheoscopy and laryngoscopy

Outpatient	Inpatient	Dutch Description	French Description
257670	257681	Stroboscopisch onderzoek van de trillingen van de stembanden	Examen stroboscopique des vibrations des cordes vocales
258274	258285	Stroboscopisch onderzoek van de stembanden met een onbuigzaam optisch systeem of door fibroscopie, met of zonder registreren van de bewegingen met een camera en vidéorecorder	Examen stroboscopique des cordes vocales à l'aide d'un système optique rigide ou par fibroscopie avec ou sans enregistrement des mouvements avec caméra et magnétoscope
471612	471623	Tracheoscopie met verwijderen van tumors en/of coagulatie van letsels	Trachéoscopie avec ablation de tumeurs et/ou coagulation de lésions
351035	351046	01/04/1985: Tracheoscopie, met of zonder afname voor biopsie	01/04/1985 : Trachéoscopie, avec ou sans prélèvement biopsique
		01/10/2008: Tracheo- en/of laryngoscopie, met of zonder afname voor biopsie	01/10/2008 : Trachéo- et/ou laryngoscopie, avec ou sans prélèvement biopsique
258075	258086	Microlaryngoscopie in suspensie (Kleinsasser) met of zonder afname voor biopsie	Microlaryngoscopie en suspension (Kleinsasser) avec ou sans prélèvement biopsique

Table 32 – Nomenclature codes bronchoscopy

Outpatient	Inpatient	Dutch Description	French Description
257294	257305	Bronchoscopie zonder afname voor biopsie en/of bronchoscopie met therapeutische aspiratie	Bronchoscopie sans prélèvement biopsique, et/ou bronchoscopie avec aspiration thérapeutique
257316	257320	Bronchoscopie met afname voor biopsie en/of verwijderen van tumors en/of coagulatie van letsel	Bronchoscopie avec prélèvement biopsique, et/ou ablation de tumeurs, et/ou coagulation de lésions
471715	471726	Bronchoscopie zonder afname voor biopsie	Bronchoscopie sans prélèvement biopsique
471730	471741	Bronchoscopie met afname voor biopsie, en/of verwijderen van tumors, en/of coagulatie van letsels	Bronchoscopie avec prélèvement biopsique, et/ou ablation de tumeurs, et/ou coagulation de lésions
471752	471763	Bronchoscopie met transcarinale punctie en eventuele radioscopische controle	Bronchoscopie avec ponction transcarinale et contrôle radioscopique éventuel
471774	471785	Bronchoscopie met bronchoalveolair wassen (min 100ml)	Bronchoscopie avec lavage broncho-alvéolaire (minimum 100 ml)
471811	471822	Bronchoscopie met perifere pulmonaire afnamen voor biopsie (ofwel veelvuldige afnamen, minimum 5, ofwel geleide afname in geval van perifere tumor), inclusief de eventuele radioscopische controle	Bronchoscopie avec prélèvement de biopsies pulmonaires périphériques (soit prélèvements multiples minimum 5, soit prélèvement dirigé en cas de tumeur périphérique) y compris le contrôle radioscopique éventuel

Table 33 – Nomenclature codes nasal endoscopy

Outpatient	Inpatient	Dutch Description	French Description
258834	258845	Nasale endoscopie met of zonder biopsie, met behulp van een rechte optiek of hoekoptiek of van een fibroscoop waarmee het cavum, de meatus, de conchae en de drainagewegen van de maxillaire, frontale, ethmoidale, sphenoïdale sinussen worden geëxploreerd inclusief de eventuele lokale anesthesie	Endoscopie nasale avec ou sans biopsie à l'aide d'une optique droite ou angulaire ou d'un fibroscope explorant le cavum, les méats, les cornets et des voies de drainage des sinus maxillaires frontaux, ethmoïdaux, sphénoïdaux, y compris l'anesthésie locale éventuelle

Appendix 3.1.4. Codes for screening digestive tract

Table 34 – Nomenclature codes screening digestive tract

Outpatient	Inpatient	Dutch Description	French Description
472356	472360	01/04/1997: Oesofagoscopie	01/04/1997 : Oesophagoscopie
		01/11/2016: Onderzoek van de oesophagus door middel van endoscopie	01/11/2016 : Examen de l' oesophage par endoscopie
472555	472566	Oesofagoscopie met wegnemen van tumors en/of coagulatie van letsels (geschrapt 01/11/2016)	Oesophagoscopie avec ablation de tumeurs et/ou coagulation de lésions (supprimé le 01/11/2016)
472415	472426	Fibrogastroscopie en/of fibrobulboscopie (geschrapt 01/11/2016)	Fibro-gastroscopie et/ou fibro-bulboscopie (supprimé le 01/11/2016)
472570	472581	Fibrogastroscopie en/of fibrobulboscopie met wegnemen van tumors en/of coagulatie van letsels (geschrapt 01/11/2016)	Fibro-gastroscopie et/ou fibro-bulboscopie avec ablation de tumeurs et/ou coagulation de lésions (supprimé le 01/11/2016)
473056	473060	Fibroduodenoscopie (2de en 3de duodenum)	Fibro-duodénoscopie (2ème et 3ème duodénum)
		01/11/2016: Onderzoek van het hogere spijsverteringskanaal door middel van endoscopie	01/11/2016: Examen du tube digestif supérieur par endoscopie
311975	311986	Speekselklierbiopsie	Biopsie d'une glande salivaire

Appendix 3.1.5. *Codes for histopathology*

Table 35 – Nomenclature codes biopsy primary tumour for oral cavity and oropharynx

Outpatient	Inpatient	Dutch Description	French Description
532011	532022	01/07/1986: Afname en fixatie van een dermo-epidermaal bioptisch fragment, zonder hechten, met het oog op een pathologisch-anatomisch onderzoek	01/07/1986 : Prélèvement et fixation d'un fragment biopsique dermoépidermique sans suture, en vue d'un examen anatomo-pathologique
532114	532125	01/07/1986: Afname en fixatie van een dermo-epidermaal bioptisch fragment, met hechten, met het oog op een pathologisch-anatomisch onderzoek	01/07/1986 : Prélèvement et fixation d'un fragment biopsique dermoépidermique avec suture, en vue d'un examen anatomo-pathologique
311953	311964	Tongbiopsie	Biopsie de la langue
588011	588022	01/07/1999: Honorarium voor het pathologisch-anatomische onderzoek door inclusie en coupe van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen en met inbegrip van het eventueel macroscopisch onderzoek van operatiestukken, voor die prelevementen die niet overeenkomen met de prestaties 588232 - 588243, 588254 - 588265, 588276 - 588280 of 588291 - 588302	01/07/1999 : Honoraires pour l'examen anatomo-pathologique par inclusion et coupe d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires, pour les prélèvements ne correspondant pas aux prestations 588232 - 588243, 588254 - 588265, 588276 - 588280 ou 588291 - 588302
588114	588125	01/07/1999: Pathologisch-anatomisch onderzoek met een elektronenmicroscoop, ongeacht de aangewende techniek of technieken, ongeacht het aantal afnamen	01/07/1999 : Examen anatomo-pathologique avec microscope électronique quelle(s) que soi(en)t la ou les technique(s) utilisée(s), quel que soit le nombre de prélèvements
588254	588265	Honorarium voor het pathologisch-anatomisch onderzoek door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek, voor volgende prelevementen: Biopten van volgende diepe organen: - lever, - nier, - nierbekken, - bijnier, - prostaat, - borst, - lymfeklier, - beenmerg, - bot, - schildklier, - speekselklier, - pleura, - long, - testikel, - peritoneum, - retroperitoneum, - mediastinum, - hersenen	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, et y compris l'examen macroscopique éventuel, pour les prélèvements suivants : Biopsies des organes profonds suivants : - foie, - rein, - bassinet, - surrénale, - prostate, - sein, - ganglion lymphatique, - moelle osseuse, - os, - glande thyroïde, - glande salivaire, - plèvre, - poumon, - testicule, - péritoine, - rétropéritoine, - médiastin, - cerveau
588276	588280	Honorarium voor het pathologisch-anatomisch onderzoek, door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek voor volgende operatiestukken: - lymfeklierexerese, - eenzijdige lymfeklier okselevidement, - eenzijdige lymfeklier liesevidement, - heelkundige longbiopsie, - totale of partiële thymectomie, - resectie van	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires suivantes : - exérèse de ganglion lymphatique, - évidement ganglionnaire axillaire unilatéral, - évidement ganglionnaire inguinal unilatéral - biopsie pulmonaire chirurgicale, - thymectomie totale ou

Outpatient	Inpatient	Dutch Description	French Description
		subaponeurotische tumoren, - partiële pancreatectomie, - partiële hepatectomie, - cholecystectomie, - splenectomie, - mesenteriale tumorectomie, - retroperitoneale tumorectomie, - oogbol resectie, - speekselklierresectie (met uitzondering van de accessoire speekselklieren), - partiële of totale glossectomie, - thyroidectomie, - parathyroidectomie, - pharyngectomie, - ncisionele borstbiopsie, - borsttumorectomie, - partiële cystectomie (met uitzondering van de endoscopische blaasresectie), - heelkundige of endoscopische prostaatadenomectomie, - epididymectomie, - orchidectomie, - partiële penis amputatie, - diepe hals tumorectomie, - partiële nefrectomie, - uni- of bilaterale adnexectomie, - ovariectomie, - totale salpingectomie, - partiële vulvectomie, - baarmoederhals conisatie of -resectie, - bijnier resectie, - zenuwbiopsie, - spierbiopsie, - hersen-, ruggemerg- of hypofyse- tumor resectie, - bottumor resectie, -tonsillectomie (>18 jaar), - adenoidectomie (>18 jaar)	partielle, - résection de tumeur subaponévrotique, - pancréatectomie partielle, - hépatectomie partielle, - cholécystectomie , - splénectomie, - tumorectomie mésentérique, - tumorectomie rétropéritonéale, - résection du globe oculaire, - résection d'une glande salivaire (à l'exception des glandes salivaires accessoires), - glossectomie partielle ou totale, - thyroïdectomie,- parathyroïdectomie, - pharyngectomie, - biopsie par incision du sein, - tumorectomie du sein, - cystectomie partielle (à l'exception de la résection vésicale endoscopique), - adénomectomie prostatique chirurgicale ou endoscopique , - épididymectomie, - orchidectomie, - amputation partielle du pénis, - tumorectomie profonde du cou, - néphrectomie partielle, - annexectomie uni-ou bilatérale, - ovariectomie, - salpingectomie totale, - vulvectomie partielle, - conisation ou résection du col de l'utérus, - résection de la glande surrénale, - biopsie nerveuse- biopsie musculaire, - résection d'une tumeur du cerveau, de la moelle épinière ou de l'hypophyse, - résection de tumeur osseuse, - amygdalectomie (> 18 ans), - adénoïdectomie (>18 ans)
588291	588302	Honorarium voor het pathologisch-anatomisch onderzoek, door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen en met inbegrip van het eventueel macroscopisch onderzoek, voor volgende operatiestukken: - partiële mammectomie met okselklier uitruiming, - totale mammectomie met of zonder okselklier uitruiming, - partiële of totale pneumectomie, - partiële of totale slokdarmresectie, - bilaterale lies klierevidement, - lymfeklierevidement van 2 of meerdere groepen halsklieren, - tumorectomie van de mondbodem met of zonder mandibulectomie, - tumorectomie van het verhemelte met of zonder maxillectomie, - totale maxillectomie, - partiële of totale gastrectomie, - dunne darm resectie, - partiële of totale colectomie, - duodenopancreatectomie, - radicale, totale of subtotale hysterectomie, - abdominoperineale resectie, - partiële of totale laryngectomie, - totale cystectomie, - totale penisamputatie, - totale nefrectomie, - totale prostatectomie (met zaadblaasjes), - hartresectie, - hart long blok, - totale hepatectomie, - totale pelvectomie, - totale vulvectomie, - foetus van 14 tot en met 24 weken	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe d'autant de prélèvements que nécessaire quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires suivantes : - mammectomie partielle avec évidement ganglionnaire, - mammectomie totale avec ou sans évidement ganglionnaire, - pneumectomie partielle ou totale, - résection partielle ou totale de l'oesophage, - évidement ganglionnaire inguinal bilatéral, - évidement de deux ou plusieurs groupes de ganglions du cou, - tumorectomie du plancher buccal avec ou sans mandibulectomie, - tumorectomie du palais avec ou sans maxillectomie, - maxillectomie totale, - gastrectomie partielle ou totale, - résection de l'intestin grêle, - colectomie partielle ou totale, - duodénopancréatectomie, - hystérectomie radicale, totale ou subtotale, - résection abdominopérinéale, - laryngectomie partielle ou totale, - cystectomie totale, - amputation totale du pénis, - néphrectomie totale, - prostatectomie totale (avec vésicules séminales), - résection cardiaque, - bloc coeur poumons complet, - hépatectomie totale, - pelvectomie totale, - vulvectomie totale, - foetus de 14 à 24 semaines y compris

Outpatient	Inpatient	Dutch Description	French Description
588070	588081	01/07/1999: Immunohistologische onderzoeken (maximum 4 per afname) voor het aantonen van antigenen in de coupes, na incubatie met antisera, per gebruikt antiserum	01/07/1999 : Examens immunohistologiques (maximum 4 par prélèvement) pour révéler des antigènes sur des coupes, après incubation d'anticorps, par anti-sérum
588976	588980	01/07/2009: Honorarium voor de immunohistologische onderzoeken voor het aantonen van farmaco-diagnostiche antigenen in de coupes na incubatie met antisera, per gebruikt antiserum, in het kader van het voorschrijven van tumor-specifieke medicatie bij oncologische patiënten	01/07/2009: Honoraires pour les examens immuno-histologiques pour la mise en évidence d'antigènes pharmaco-diagnostiques au niveau des coupes, après incubation avec antisérums, par antisérum utilisé, dans le cadre de la prescription d'une médication spécifique à la tumeur pour des patients oncologiques
588033	588044	01/07/1999: Peroperatoir pathologisch-anatomisch extempore onderzoek, ongeacht het aantal afnamen volgens de vriesmethode en ongeacht het aantal verrichte controle-onderzoeken na inclusie en coupe	01/07/1999 : Examen peropératoire extemporané quel que soit le nombre de prélèvements examinés par la technique de congélation et quel que soit le nombre de contrôles effectués après inclusion et coupe
588232	588243	Honorarium voor het pathologisch-anatomisch onderzoek door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek voor volgende prelevementen - vagotomie - vasectomie - tuba-ligatuur - tonsillectomie (< 18 jaar) - adenoidectomie (< 18 jaar) - sympathectomie	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, et y compris l'examen macroscopique éventuel, pour les prélèvements suivants : - vagotomie - vasectomie - ligature tubaire - amygdalectomie (< 18 ans) - adenoidectomie (<18 ans) - sympathectomie

Table 36 – Nomenclature codes biopsy primary tumour for hypopharynx and larynx

Outpatient	Inpatient	Dutch Description	French Description
588011	588022	01/07/1999: Honorarium voor het pathologisch-anatomische onderzoek door inclusie en coupe van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen en met inbegrip van het eventueel macroscopisch onderzoek van operatiestukken, voor die prelevementen die niet overeenkomen met de prestaties 588232 - 588243, 588254 - 588265, 588276 - 588280 of 588291 - 588302	01/07/1999 : Honoraires pour l'examen anatomo-pathologique par inclusion et coupe d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires, pour les prélèvements ne correspondant pas aux prestations 588232 - 588243, 588254 - 588265, 588276 - 588280 ou 588291 - 588302
588114	588125	01/07/1999: Pathologisch-anatomisch onderzoek met een elektronenmicroscoop, ongeacht de aangewende techniek of technieken, ongeacht het aantal afnamen	01/07/1999 : Examen anatomo-pathologique avec microscope électronique quelle(s) que soi(en)t la ou les technique(s) utilisée(s), quel que soit le nombre de prélèvements
588254	588265	Honorarium voor het pathologisch-anatomisch onderzoek door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek, voor volgende prelevementen: Biopten van volgende diepe organen: - lever, - nier, - nierbekken, - bijnier, - prostaat, - borst, - lymfeklier, - beenmerg, - bot, - schildklier, - speekselklier, - pleura, - long, - testikel, - peritoneum, - retroperitoneum, - mediastinum, - hersenen	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, et y compris l'examen macroscopique éventuel, pour les prélèvements suivants : Biopsies des organes profonds suivants : - foie, - rein, - bassinet, - surrénale, - prostate, - sein, - ganglion lymphatique, - moelle osseuse, - os, - glande thyroïde, - glande salivaire, - plèvre, - poumon, - testicule, - péritoine, - rétropéritoine, - médiastin, - cerveau
588276	588280	Honorarium voor het pathologisch-anatomisch onderzoek, door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek voor volgende operatiestukken: - lymfeklierexerese, - eenzijdige lymfeklier okselevidement, - eenzijdige lymfeklier liesevidement, - heelkundige longbiopsie, - totale of partiële thymectomie, - resectie van subaponeurotische tumoren, - partiële pancreatectomie, - partiële hepatectomie, - cholecystectomie, - splenectomie, - mesenteriale tumorectomie, - retroperitoneale tumorectomie, - oogbol resectie, - speekselklierresectie (met uitzondering van de accessoire speekselklieren), - partiële of totale glossectomie, - thyroidectomie, - parathyroidectomie, - pharyngectomie, - ncisionele borstbiopsie, - borsttumorectomie, - partiële cystectomie (met uitzondering van de endoscopische blaasresectie), - heelkundige of endoscopische prostaatadenomectomie, - epididymectomie, - orchidectomie, - partiële penis amputatie, - diepe hals tumorectomie, - partiële nefrectomie, - uni- of bilaterale adnexectomie, - ovariectomie, - totale salpingectomie, -	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires suivantes : - exérèse de ganglion lympathique, - évidement ganglionnaire axillaire unilatéral, - évidement ganglionnaire inguinal unilatéral - biopsie pulmonaire chirurgicale, - thymectomie totale ou partielle, - résection de tumeur subaponévrotique, - pancréatectomie partielle, - hépatectomie partielle, - cholécystectomie , - splénectomie, - tumorectomie mésentérique, - tumorectomie rétropéritonéale, - résection du globe oculaire, - résection d'une glande salivaire (à l'exception des glandes salivaires accessoires), - glossectomie partielle ou totale, - thyroïdectomie,- parathyroïdectomie, - pharyngectomie, - biopsie par incision du sein, - tumorectomie du sein, - cystectomie partielle (à l'exception de la résection vésicale endoscopique), - adénomectomie prostatique chirurgicale ou endoscopique, - épididymectomie, - orchidectomie, - amputation partielle du pénis, - tumorectomie profonde du cou, - néphrectomie partielle, -

Outpatient	Inpatient	Dutch Description	French Description
		partiële vulvectomie, - baarmoederhals conisatie of -resectie, - bijnier resectie, - zenuwbiopsie, - spierbiopsie, - hersen-, ruggemerg- of hypofyse- tumor resectie, - bottumor resectie, -tonsillectomie (>18 jaar), - adenoidectomie (>18 jaar)	annexectomie uni-ou bilatérale, - ovariectomie, - salpingectomie totale, - vulvectomie partielle, - conisation ou résection du col de l'utérus, - résection de la glande surrénale, - biopsie nerveuse- biopsie musculaire, - résection d'une tumeur du cerveau, de la moelle épinière ou de l'hypophyse, - résection de tumeur osseuse, - amygdalectomie (> 18 ans), - adénoïdectomie (>18 ans)
588291	588302	Honorarium voor het pathologisch-anatomisch onderzoek, door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen en met inbegrip van het eventueel macroscopisch onderzoek, voor volgende operatiestukken: - partiële mammectomie met okselklier uitruiming, - totale mammectomie met of zonder okselklier uitruiming, - partiële of totale pneumectomie, - partiële of totale slokdarmresectie, - bilaterale lies klierevidement, - lymfeklierevidement van 2 of meerdere groepen halsklieren, - tumorectomie van de mondbodem met of zonder mandibulectomie, - tumorectomie van het verhemelte met of zonder maxillectomie, - totale maxillectomie, - partiële of totale gastrectomie, - dunne darm resectie, - partiële of totale colectomie, - duodenopancreatectomie, - radicale, totale of subtotale hysterectomie, - abdominoperineale resectie, - partiële of totale laryngectomie, - totale cystectomie, - totale penisamputatie, - totale nefrectomie, - totale prostatectomie (met zaadblaasjes), - hartresectie, - hart long blok, - totale hepatectomie, - totale pelvectomie, - totale vulvectomie, - foetus van 14 tot en met 24 weken	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe d'autant de prélèvements que nécessaire quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, y compris l'examen macroscopique éventuel des pièces opératoires suivantes : - mammectomie partielle avec évidement ganglionnaire, - mammectomie totale avec ou sans évidement ganglionnaire, - pneumectomie partielle ou totale, - résection partielle ou totale de l'oesophage, - évidement ganglionnaire inguinal bilatéral, - évidement de deux ou plusieurs groupes de ganglions du cou, - tumorectomie du plancher buccal avec ou sans mandibulectomie, - tumorectomie du palais avec ou sans maxillectomie, - maxillectomie totale, - gastrectomie partielle ou totale, - résection de l'intestin grêle, - colectomie partielle ou totale, - duodénopancréatectomie, - hystérectomie radicale, totale ou subtotale, - résection abdominopérinéale, - laryngectomie partielle ou totale, - cystectomie totale, - amputation totale du pénis, - néphrectomie totale, - prostatectomie totale (avec vésicules séminales), - résection cardiaque, - bloc coeur poumons complet, - hépatectomie totale, - pelvectomie totale, - vulvectomie totale, - foetus de 14 à 24 semaines y compris
588070	588081	01/07/1999: Immunohistologische onderzoeken (maximum 4 per afname) voor het aantonen van antigenen in de coupes, na incubatie met antisera, per gebruikt antiserum	01/07/1999 : Examens immunohistologiques (maximum 4 par prélèvement) pour révéler des antigènes sur des coupes, après incubation d'anticorps, par anti-sérum
588976	588980	01/07/2009: Honorarium voor de immunohistologische onderzoeken voor het aantonen van farmaco-diagnostiche antigenen in de coupes na incubatie met antisera, per gebruikt antiserum, in het kader van het voorschrijven van tumor-specifieke medicatie bij oncologische patiënten	01/07/2009: Honoraires pour les examens immuno-histologiques pour la mise en évidence d'antigènes pharmaco-diagnostics au niveau des coupes, après incubation avec antisérums, par antisérum utilisé, dans le cadre de la prescription d'une médication spécifique à la tumeur pour des patients oncologiques
588033	588044	01/07/1999: Peroperatoir pathologisch-anatomisch extempore onderzoek, ongeacht het aantal afnamen volgens de vriesmethode en	01/07/1999 : Examen peropératoire extemporané quel que soit le nombre de prélèvements examinés par la technique de congélation et quel que soit le nombre de contrôles effectués après inclusion et coupe

Outpatient	Inpatient	Dutch Description	French Description
		ongeacht het aantal verrichte controle-onderzoeken na inclusie en coupe	
588232	588243	Honorarium voor het pathologisch-anatomisch onderzoek door inclusie en coupe, van zoveel prelevementen als nodig, ongeacht het aantal coupes en ongeacht het aantal onderzochte organen, en met inbegrip van het eventueel macroscopisch onderzoek voor volgende prelevementen - vagotomie - vasectomie - tuba-ligatuur - tonsillectomie (< 18 jaar) - adenoidectomie (< 18 jaar) - sympathectomie	Honoraires pour l'examen anatomo-pathologique par inclusion et coupe, d'autant de prélèvements que nécessaire, quel que soit le nombre de coupes et quel que soit le nombre d'organes examinés, et y compris l'examen macroscopique éventuel, pour les prélèvements suivants : - vagotomie - vasectomie - ligature tubaire - amygdalectomie (< 18 ans) - adenoidectomie (<18 ans) - sympathectomie
256594	256605	Bioptische afname van de larynx	Prélèvement biopsique du larynx
258075	258086	Microlaryngoscopie in suspensie (Kleinsasser) met of zonder afname voor biopsie	Microlaryngoscopie en suspension (Kleinsasser) avec ou sans prélèvement biopsique
258090	258101	Endoscopische heelkunde op de larynx: Cordectomie, cordopexie, arytenoïdectomie, arytenoïdopexie	Chirurgie endoscopique du larynx : Cordectomie, cordopexie, aryténoïdectomie, aryténoïdopexie
258112	258123	01/10/1995: Endoscopische heelkunde op de larynx: andere gevallen dan die omschreven in de verstrekking 258090 - 258101	01/10/1995 : Chirurgie endoscopique du larynx : autres cas que ceux décrits dans la prestation 258090 - 258101
		01/05/2009: Endoscopische heelkunde op de larynx: andere gevallen dan die omschreven in de verstrekking 258090 - 258101 of 258871-258882	01/05/2009 : Chirurgie endoscopique du larynx : autres cas que ceux décrits dans la prestation 258090 - 258101 ou 258871-258882

Table 37 – Nomenclature codes lymph node biopsy

Outpatient	Inpatient	Dutch Description	French Description
258311	258322	Excisie voor biopsie van een oppervlakkige halsklier	Excision pour biopsie d'un ganglion superficiel du cou
258333	258344	Excisie voor biopsie van een diep gelegen halsklier	Excision pour biopsie d'un ganglion profond du cou
312513	312524	Excisie voor biopsie van een oppervlakkige halsklier	Excision pour biopsie d'un ganglion superficiel du cou
312535	312546	Excisie voor biopsie van een diep gelegen halsklier	Excision pour biopsie d'un petit ganglion profond du cou
355692	355703	Punctie van hematopoeitisch orgaan, exclusief lever en milt	Ponction d'un organe hématopoïétique, à l'exclusion du foie et de la rate
220356	220360	Exeresis van ganglion	Exérèse ganglionnaire
a588394	588405	Honorarium voor het cytopathologisch onderzoek voor het opzoeken van neoplastische cellen (zowel na uitstrijken en/of insluiten), op urinestalen en/of sputumstalen, ongeacht het aantal uitstrijkpreparaten en/of insluiten	Honoraires pour l'examen cytopathologique pour la recherche de cellules néoplasiques (après frottis et/ou inclusion), sur échantillons d'urine et/ou d'expectoration, quel que soit le nombre de frottis et/ou d'inclusions
588416	588420	01/07/1999: Honorarium voor het cytopathologisch onderzoek voor het opzoeken van neoplastische cellen (zowel na uitstrijken en/of insluiten), van afnamen niet gespecificeerd in de verstrekkingen 588350 - 588361 en 588394 - 588405, ongeacht het aantal uitstrijkpreparaten en/of insluiten per afname	01/07/1999: Honoraires pour l'examen cytopathologique pour la recherche de cellules néoplasiques (après frottis et/ou inclusion), de prélèvements non précisés dans les prestations 588350 - 588361 et 588394 - 588405, quel que soit le nombre de frottis et/ou d'inclusions, par prélèvement
		01/04/2018: Honorarium voor het cytopathologisch onderzoek voor het opzoeken van neoplastische cellen (zowel na uitstrijken en/of insluiten), van afnamen niet gespecificeerd in de verstrekkingen 589853-589864 en 588394 - 588405, ongeacht het aantal uitstrijkpreparaten en/of insluiten, per afname	01/04/2018: Honoraires pour l'examen cytopathologique pour la recherche de cellules néoplasiques (après frottis et/ou inclusion), de prélèvements non précisés dans les prestations 589853-589864 et 588394 - 588405, quel que soit le nombre de frottis et/ou d'inclusions, par prélèvement

Appendix 3.2.   Nomenclature codes for surgery with curative intent

Different types of surgical procedures are taken into account: minor surgery, major surgery, lymphadenectomy and reconstructive surgery to define the surgery with curative intent. An algorithm was constructed that took the different types of surgery into account (see section 3.3.2).

Appendix 3.2.1. Oral Cavity

Minor surgical procedures

Table 38 – Nomenclature codes 'minor surgical procedures' SCC of the oral cavity

Outpatient	Inpatient	K-value	Dutch Description	French Description
256572	256583	30	Wegnemen van huigtumor	Ablation de tumeur de la luette
317111	317122	10	Exeresis van goedaardige intrabuccale tumors	Exérèse de tumeurs intrabuccales bénignes

Major surgical procedures

Table 39 – Nomenclature codes 'major surgical procedures' SCC of the oral cavity

Outpatient	Inpatient	K-value	Dutch Description	French Description
256115	256126	120	Heelkundige bewerking wegens tumor van de tandkasrand	Intervention chirurgicale pour tumeur du rebord alvéolo-dentaire
256196	256200	120	Gedeeltelijke tongresectie buiten de traumatische letsels	Résection partielle de la langue en dehors des lésions traumatiques
310590	310601	120	Gedeeltelijke tongresectie buiten de traumatische letsels	Résection partielle de la langue en dehors des lésions traumatiques
256336	256340	120	Heelkundige bewerking wegens tumor van mondbodem	Intervention chirurgicale pour tumeur du plancher de la bouche
258451	258462	400	Heelkundig verwijderen van een expansief diepliggend letsel dat een resectie van een deel van de schedelbasis noodzakelijk maakt	Ablation chirurgicale d'une lésion expansive profonde nécessitant la résection d'une partie de la base du crâne

Outpatient	Inpatient	K-value	Dutch Description	French Description
312653	312664	400	Heelkundig verwijderen van een expansief diepliggend letsel dat een resectie van een deel van de schedelbasis noodzakelijk maakt	Ablation chirurgicale d'une lésion expansive profonde nécessitant la résection d'une partie de la base du crâne
259033	259044	400	Resectie van een expansief letsel van de luchtwegen en/of van het bovenste gedeelte van het spijsverteringskanaal dat het sluiten van een huid- of slijmvliesdefect met een huidlap, een myocutane of een wandelende ent vereist	Résection d'une lésion expansive des voies respiratoires et/ou des voies digestives supérieures nécessitant la fermeture d'un défect cutané ou muqueux par un lambeau cutané, myocutané ou une greffe libre
259114	259125	400	Transmandibulaire buccofaryngectomie of glossopelvimandibulectomie	Buccopharyngectomie transmandibulaire ou glossopelvimandibulectomie
311010	311021	120	Gedeeltelijke resectie zonder discontinuïteit van onderkaakbeen	Résection partielle n'entraînant pas la discontinuité du maxillaire inférieur
311032	311043	180	Gedeeltelijke resectie met discontinuïteit van onderkaakbeen of resectie van kinstreek	Résection partielle entraînant la discontinuité du maxillaire inférieur ou résection de la région mentonnière
311091	311102	225	Volledige resectie van onderkaakbeen	Résection complète du maxillaire inférieur
311150	311161	180	Subtotale maxillectomie met resectie van de alveolaire kam en het verhemelte	Maxillectomie sub-totale avec résection du rebord alvéolaire et du palais
311172	311183	225	Totale maxillectomie met inbegrip van de oogkasbodem en/of processi ptergyoidei	Maxillectomie totale y compris le fond de l'orbite et/ou les apophyses ptérygoïdes de l'os sphénoïdal
311312	311323	120	1/04/1985: Ingreep wegens tumor op alveolodentale rand	01/04/1985 : Intervention pour tumeur du rebord alvéolo-dentaire
			1/05/2009: Heelkundige ingreep wegens tumor op de tandkasrand	01/05/2009 : Intervention chirurgicale pour tumeur du rebord alvéolo-dentaire
312690	312701	250	1/07/1986: Subtotale maxillectomie met resectie van de alveolaire kam en het verhemelte met huidgreffe, in eenzelfde operatietijd	01/07/1986 : Maxillectomie sub-totale avec résection du rebord alvéolaire et du palais avec greffe de peau, dans un même temps opératoire
			01/05/2009: Subtotale maxillectomie met resectie van de alveolaire kam en het verhemelte (geschrapt op 1/02/2011)	01/05/2009 : Maxillectomie subtotale avec résection du rebord alvéolaire et du palais (supprimé le 01/02/2011)
312712	312723	300	1/07/1986: Totale maxillectomie met inbegrip van de oogkasbodem en/of processi ptergygoidei met huidgreffe, in eenzelfde operatietijd	01/07/1986 : Maxillectomie totale, y compris le fond de l'orbite et/ou les apophyses ptérygoïdes de l'os sphénoïdal, avec greffe de peau, dans un même temps opératoire
			1/05/2009: Totale maxillectomie met inbegrip van de oogkasbodem en/of processi pterygoidei van het sfenoid (geschrapt op 1/02/2011)	01/05/2009 : Maxillectomie totale y compris le fond de l'orbite et/ou les apophyses ptérygoïdes de l'os sphénoïdal (supprimé le 01/02/2011)

Outpatient	Inpatient	K-value	Dutch Description	French Description
310951	310962	180	Trepanatie van kaakbeen wegens cystische tumor of ostitis	Trépanation du maxillaire pour tumeur kystique ou ostéite
251731	251742	163,35	Verwijderen van een gezwel van de huid of de slijmvliezen of ander letsel rechtstreeks toegankelijk door excisie met plastie en/of greffe	Exérèse d'une tumeur de la peau ou des muqueuses ou d'une autre lésion directement accessible, par excision avec plastie et/ou greffe
251753	251764	240	Verwijderen van een kwaadaardig gezwel van de huid of de slijmvliezen volgens een micrografische heelkundige techniek met peroperatieve pathologische anatomie, zonder sluiten van de wonde	Exérèse d'une tumeur maligne de la peau ou des muqueuses selon une technique de chirurgie micrographique avec examen anatomo-pathologique peropératoire, sans fermeture de la plaie
251775	251786	300	Verwijderen van een kwaadaardig gezwel van de huid of de slijmvliezen volgens een micrografische heelkundige techniek met peroperatieve pathologische anatomie, en met sluiten van de wonden, een eventuele ent en/of plastie inbegrepen	Exérèse d'une tumeur maligne de la peau ou des muqueuses selon une technique de chirurgie micrographique avec examen anatomo-pathologique peropératoire, et avec fermeture de la plaie, y compris une greffe et/ou plastie éventuelle
220312	220323	120	Heelkundige bewerking wegens expansieve diepe tumoren of letsels aan het gelaat of lippen die brede resectie vergt, inclusief plastiek	Intervention chirurgicale pour tumeurs profondes ou lésions de la face ou des lèvres, à l'exclusion des lésions cutanées
220334	220345	180	Heelkundige bewerking wegens diepe tumoren of letsels aan het gelaat of lippen, exclusief huidletsels	Intervention chirurgicale pour tumeurs profondes ou lésions de la face ou des lèvres, à l'exclusion des lésions cutanées
220275	220286	120	05/06/1985: exerese van onder de aponeurose gelegen expansieve tumoren uit de weke delen	05/06/1985: Exérèse de tumeurs expansives situées sous l'aponévrose dans les parties molles
			01/05/2007: Exerese van een onder de aponeurose gelegen expansieve tumor uit de weke weefsels	01/05/2007: Exérèse d'une tumeur sous-aponévrotique expansive des tissus mous
471612	471623	70	Tracheoscopie met verwijderen van tumors en/of coagulatie van letsels	Trachéoscopie avec ablation de tumeurs et/ou coagulation de lésions

Appendix 3.2.2. Oropharynx

Minor surgical procedures

Table 40 – Nomenclature codes 'minor surgical procedures' SCC of the oropharynx

Outpatient	Inpatient	K-value	Dutch Description	French Description
256535	256546	100	Amygdalectomie, met of zonder adenoïdectomie, bij volwassenen, d.w.z. degene die achttien jaar is of ouder	Amygdalectomie, avec ou sans adénoïdectomie, chez l'adulte, c'est-à-dire la personne qui a atteint ou dépassé le jour anniversaire de ses dix-huit ans
257390	257401	100	Amygdalectomie door dissectie	Amygdalectomie à la dissection
258576	258580	180	Uvuloplastie met of zonder amygdalectomie	Uvuloplastie avec ou sans amygdalectomie
310590	310601	120	Gedeeltelijke tongresectie buiten de traumatische letsels	Résection partielle de la langue en dehors des lésions traumatiques
256196	256200	120	Gedeeltelijke tongresectie buiten de traumatische letsels	Résection partielle de la langue en dehors des lésions traumatiques
256336	256340	120	Heelkundige bewerking wegens tumor van de mondbodem	Intervention chirurgicale pour tumeur du plancher de la bouche
220312	220323	120	Heelkundige bewerking wegens diepe tumoren of letsels aan het gelaat of lippen, exclusief huidletsels	Intervention chirurgicale pour tumeurs profondes ou lésions de la face ou des lèvres, à l'exclusion des lésions cutanées
220334	220345	180	Heelkundige bewerking wegens expansieve diepe tumoren of letsels aan het gelaat of lippen die brede resectie vergt, inclusief plastiek	Intervention chirurgicale pour tumeurs profondes expansives ou lésions de la face ou des lèvres, nécessitant résection large, plastique comprise
311312	311323	120	01/04/1985: Ingreep wegens tumor op alveolodentale rand	01/04/1985 : Intervention pour tumeur du rebord alvéolo-dentaire
			01/05/2009: Heelkundige ingreep wegens tumor op de tandkasrand	01/05/2009 : Intervention chirurgicale pour tumeur du rebord alvéolo-dentaire
220275	220286	120	05/06/1985: Exerese van onder de aponeurose gelegen expansieve tumoren uit de weke delen (05/06/1985)	05/06/1985: Exérèse de tumeurs expansives situées sous l'aponévrose dans les parties molles (05/06/1985)
			01/05/2007: Exerese van een onder de aponeurose gelegen expansieve tumor uit de weke weefsels	01/05/2007: Exérèse d'une tumeur sous-aponévrotique expansive des tissus mous
251786	251775	300	Verwijderen van een kwaadaardig gezwel van de huid of de slijmvliezen volgens een micrografische heelkundige techniek	Exérèse d'une tumeur maligne de la peau ou des muqueuses selon une technique de chirurgie micrographique avec examen

Outpatient	Inpatient	K-value	Dutch Description	French Description
			met peroperative pathologische anatomie, en met sluiten van de wonden, een eventuele ent en/of plastie inbegrepen	anatomo-pathologique peropératoire, et avec fermeture de la plaie, y compris une greffe et/ou plastie éventuelle
256115	256126	120	Heelkundige ingreep wegens tumor op de tandkasrand	Intervention chirurgicale pour tumeur du rebord alvéolo-dentaire
251731	251742	163,35	Verwijderen van een gezwel van de huid of de slijmvliezen of ander letsel rechtstreeks toegankelijk door excisie met plastie en/of greffe	Exérèse d'une tumeur de la peau ou des muqueuses ou d'une autre lésion directement accessible, par excision avec plastie et/ou greffe

Major surgical procedures

Table 41 – Nomenclature codes 'major surgical procedures' SCC of the oropharynx

Outpatient	Inpatient	K-value	Dutch Description	French Description
257191	257202	225	Faryngectomie	Pharyngectomie
258856	258860	300	01/05/2009: Transorale endoscopische faryngectomie	01/05/2009: Pharyngectomie endoscopique transorale
259033	259044	400	Resectie van een expansief letsel van de luchtwegen en/of van het bovenste gedeelte van het spijsverteringskanaal dat het sluiten van een huid- of slijmvliesdefect met een huidlap, een myocutane of een wandelende ent vereist.	Résection d'une lésion expansive des voies respiratoires et/ou des voies digestives supérieures nécessitant la fermeture d'un défect cutané ou muqueux par un lambeau cutané, myocutané ou une greffe libre
259114	259125	400	Transmandibulaire buccofaryngectomie of glossopelvimandibulectomie	Buccopharyngectomie transmandibulaire ou glossopelvimandibulectomie

Appendix 3.2.3. Hypopharynx

Minor surgical procedures

Table 42 – Nomenclature codes 'minor surgical procedures' SCC of the hypopharynx

Outpatient	Inpatient	K-value	Dutch Description	French Description
258090	258101	240	Endoscopische heelkunde op de larynx: Cordectomie, cordopexie, arytenoïdectomie, arytenoïdopexie	Chirurgie endoscopique du larynx : Cordectomie, cordopexie, aryténoïdectomie, aryténoïdopexie
258893	258904	240	01/05/2009: Endoscopische procedure voor intratumorale photodynamische behandeling of electroporatietherapie bij mucosatuomoren voor de volledige behandeling van het geheel der letsels	01/05/2009 : Procédure endoscopique pour le traitement photodynamique intratumoral ou thérapie par électroporation de tumeurs des muqueuses pour le traitement complet de l'ensemble des lésions

Major surgical procedures

Table 43 – Nomenclature codes 'major surgical procedures' SCC of the hypopharynx

Outpatient	Inpatient	K-value	Dutch Description	French Description
257191	257202	225	Pharyngectomie	Pharyngectomie
259114	259125	400	Transmandibulaire buccofaryngectomie of glossopelvimandibulectomie	Buccopharyngectomie transmandibulaire ou glossopelvimandibulectomie
258856	258860	300	01/05/2009:Transorale endoscopische faryngectomie	01/05/2009: Pharyngectomie endoscopique transorale
256771	256782	400	Volledige of gedeeltelijke horizontale laryngectomie of hemilaryngectomie	Laryngectomie totale ou partielle horizontale ou hemilaryngectomie
259033	259044	400	Resectie van een expansief letsel van de luchtwegen en/of van het bovenste gedeelte van het spijsverteringskanaal dat het sluiten van een huid- of slijmvliesdefect met een huidlap, een myocutane of een wandelende ent vereist	Résection d'une lésion expansive des voies respiratoires et/ou des voies digestives supérieures nécessitant la fermeture d'un défect cutané ou muqueux par un lambeau cutané, myocutané ou une greffe libre
256756	256760	240	Chordectomie of laryngectomie van het frontolaterale type (partiele laryngectomie)	Cordectomie ou laryngectomie de type fronto-latérale
259011	259022	400	Reconstructieve subtotale laryngectomie met het oog op het behoud van de larynxfuncties	Laryngectomie subtotale reconstructive en vue de conserver les fonctions laryngées

Outpatient	Inpatient	K-value	Dutch Description	French Description
258871	258882	400	Transorale endoscopische horizontale (supraglottis) laryngectomie of hemilaryngectomie met inbegrip van arytenoid	Laryngectomie endoscopique transorale horizontale (supraglottique) ou hémi-laryngectomie y compris l'aryténoïde
228012	228023	1100	01/04/1985 : Thoracale of thoraco-abdominale oesofagectomie of gastro-oesofagectomie in één operatietijd	01/04/1985 : Oesophagectomie ou gastro-oesophagectomie thoracique ou thoraco-abdominale, en un temps
			01/04/2011 : Thoracale of thoraco-abdominale oesofagectomie of gastro-oesofagectomie in één operatietijd met herstellen van de continuïteit	01/04/2011 : Oesophagectomie ou gastro-oesophagectomie thoracique ou thoraco-abdominale, en un temps avec reconstitution de la continuité
228174	228185	1500	Subtotale oesofagectomie tot op het niveau van de arcus aortae, met herstellen van de continuïteit	Oesophagectomie subtotale jusqu'au niveau de la crosse aortique, avec reconstitution de la continuité
228233	228244	1300	01/04/2011: Thoracale of thoraco-abdominale oesofagectomie of gastro-oesofagectomie in één operatietijd met herstellen van de continuïteit en uitgebreid klierevidement	01/04/2011: Oesophagectomie ou gastro-oesophagectomie thoracique ou thoraco-abdominale, en un temps avec reconstitution de la continuité et évidement ganglionnaire étendu

Appendix 3.2.4. Larynx

Minor surgical procedures

Table 44 – Nomenclature codes 'minor surgical procedures' SCC of the larynx

Outpatient	Inpatient	K-value	Dutch Description	French Description
258090	258101	240	Endoscopische heelkunde op de larynx: Cordectomie, cordopexie, arytenoïdectomie, arytenoïdopexie	Chirurgie endoscopique du larynx : Cordectomie, cordopexie, aryténoïdectomie, aryténoïdopexie
258893	258904	240	01/05/2009: Endoscopische procedure voor intratumorale photodynamische behandeling of electroporatietherapie bij mucosatuomoren voor de volledige behandeling van het geheel der letsels	01/05/2009: Procédure endoscopique pour le traitement photodynamique intratumoral ou thérapie par électroporation de tumeurs des muqueuses pour le traitement complet de l'ensemble des lésions

Major surgical procedures

Table 45 – Nomenclature codes 'major surgical procedures' SCC of the larynx

Outpatient	Inpatient	K-value	Dutch Description	French Description
259011	259022	400	Reconstructieve subtotale laryngectomie met het oog op het behoud van de larynxfuncties	Laryngectomie subtotale reconstructive en vue de conserver les fonctions laryngées
227275	227286	1300	01/04/1985 : Tracheobronchiale of bronchobronchiale anastomose	01/04/1985 : Anastomose trachéo-bronchique ou broncho-bronchique
			01/05/2007: Resectie met anastomose (broncho-bronchiaal of tracheo-bronchiaal) van een stambronchus of van de trachea via thoracotomie	01/05/2007 : Résection d'une bronche souche ou de la trachée avec anastomose (broncho-bronchique ou trachéo-bronchique) par thoracotomie
257456	257460	300	Heelkundige behandeling van tracheale stenose door segmentaire resectie	Traitement chirurgical de la sténose trachéale par résection segmentaire
258716	258720	120	Behandeling van een tracheale stenose door laserresectie	Traitement d'une sténose trachéale par résection au laser
256756	256760	240	Chordectomie of laryngectomie van het frontolaterale type (partiele laryngectomie)	Cordectomie ou laryngectomie de type fronto-latérale
256771	256782	400	Volledige of gedeeltelijke horizontale laryngectomie of hemilaryngectomie	Laryngectomie totale ou partielle horizontale ou hemilaryngectomie
259033	259044	400	Resectie van een expansief letsel van de luchtwegen en/of van het bovenste gedeelte van het spijsverteringskanaal dat het sluiten van een huid- of slijmvliesdefect met een huidlap, een myocutane of een wandelende ent vereist	Résection d'une lésion expansive des voies respiratoires et/ou des voies digestives supérieures nécessitant la fermeture d'un défect cutané ou muqueux par un lambeau cutané, myocutané ou une greffe libre
258871	258882	400	01/05/2009: Transorale endoscopische horizontale (supraglottis) laryngectomie of hemilaryngectomie met inbegrip van arytenoid	01/05/2009: Laryngectomie endoscopique transorale horizontale (supraglottique) ou hémi-laryngectomie y compris l'aryténoïde
258856	258860	300	01/05/2009: Transorale endoscopische faryngectomie	01/05/2009: Pharyngectomie endoscopique transorale

Appendix 3.2.5. Lymphadenectomy

Table 46 – Nomenclature codes for lymphadenectomy

Outpatient	Inpatient	Dutch Description	French Description
258392	258403	01/07/1986: Volledige halsklieruitruiming van een gebied afgelijnd door: bovenaan het mastoïd en de onderkaak, onderaan de clavicula, achteraan de M. Trapezius en vooraan de pretracheale spieren	01/07/1986 : Evidement ganglionnaire total d'une région délimitée par : en haut, la mastoïde et la mandibule, en bas, la clavicule, à l'arrière le muscle trapèze et devant les muscles prétrachéaux
		01/05/2009: Unilaterale uitruiming van 4 of meer kliergroepen in de hals met georiënteerd resectiespecimen	01/05/2009: Evidement unilatéral de 4 groupes ganglionnaires ou plus du cou avec spécimen de résection orienté
258554	258565	01/10/1995: Uitruiming van ganglia van een kliergroep in de hals	01/10/1995 : Evidement ganglionnaire d'un groupe ganglionnaire du cou
		01/05/2009: Unilaterale uitruiming van één of twee kliergroepen in de hals	01/05/2009: Evidement unilatéral d'un ou deux groupes ganglionnaires du cou
312572	312583	01/07/1986: Beperkte klieruitruiming van 2 of meerder kliergroepen in de hals	01/07/1986 : Evidement ganglionnaire restreint de 2 ou plusieurs groupes ganglionnaires du cou
		01/05/2009: Unilaterale uitruiming van 3 kliergroepen in de hals met georiënteerd resectiespecimen	01/05/2009: Evidement unilatéral de 3 groupes ganglionnaires du cou avec spécimen de résection orienté
312594	312605	01/07/1986: Volledige halsklieruitruiming van een gebied afgelijnd door: bovenaan het mastoïd en de onderkaak, onderaan de clavicula, achteraan de M. Trapezius en vooraan de pretracheale spieren	01/07/1986 : Evidement ganglionnaire totale d'une région délimitée par : en haut, la mastoïde et la mandibule, en bas, la clavicule, à l'arrière le muscle trapèze et devant les muscles prétrachéaux
		01/05/2009: Unilaterale uitruiming van 4 of meer kliergroepen in de hals met georiënteerd resectiespecimen	01/05/2009: Evidement unilatéral de 4 groupes ganglionnaires ou plus du cou avec spécimen de résection orienté
312970	312981	01/05/2009: Unilaterale uitruiming van één of twee kliergroepen in de hals	01/05/2009: Evidement unilatéral d'un ou deux groupes ganglionnaires du cou
258370	258381	01/07/1986: Beperkte klieruitruiming van 2 of meerdere kliergroepen in de hals	01/07/1986 : Evidement ganglionnaire restreint de 2 ou plusieurs groupes ganglionnaires du cou
		01/05/2009: Unilaterale uitruiming van 3 kliergroepen in de hals met georiënteerd resectiespecimen	01/05/2009: Evidement unilatéral de 3 groupes ganglionnaires du cou avec spécimen de résection orienté
256933	256944	01/04/1985: Heelkundige bewerking wegens diepliggende halscyste of -tumor	01/04/1985: Intervention chirurgicale pour kyste ou tumeur profonde du cou

Appendix 3.2.6. Reconstructive surgery

Table 47 – Nomenclature codes for reconstructive surgery

Outpatient	Inpatient	Dutch Description	French Description
251812	251823	01/04/1985: Wandelende huidlapplastiek met vasculaire pediculus, die vasculaire microsutuur impliceert	01/04/1985 : Greffe de lambeau cutané libre avec pédicule vasculaire impliquant microsuture vasculaire
		01/04/2003: Voorbereiden van bloedvaten thv receptorplaats en inzetten van de flap bij middel van microchirurgische technieken: termino-terminale arterie en vene anastomose (met of zonder zenuw anastomose)	01/04/2003 : Préparation des vaisseaux dans le site receveur, mise en place du lambeau, et réalisation des sutures microchirurgicales : sutures vasculaires simples : une artère et une anastomose veineuse (avec ou sans neuro-anastomose)
251834	251845	01/04/1985: Wandelende huidlapplastiek met neurovasculaire pediculus, die vasculaire en nerveuze microsutuur impliceert	01/04/1985 : Greffe de lambeau cutané libre avec pédicule neurovasculaire impliquant microsuture vasculaire et nerveuse
		01/04/2003: Voorbereiden van bloedvaten thv receptorplaats en inzetten van de flap bij middel van ingewikkelde microchirurgische vaatsutuur : termino-lateraal; tweeloopsanastomose	01/04/2003 : Préparation des vaisseaux dans le site receveur, mise en place du lambeau, et réalisation des sutures microchirurgicales : sutures vasculaires complexes (termino-latérales, canon de fusil..)
251856	251860	01/04/1985 Spierlap, hoofdbewerking of enige bewerking	01/04/1985 : Lambeau musculaire, temps principal ou unique
		01/04/2003: Spierlap, hoofdbewerking	01/04/2003 : Lambeau musculaire, temps principal
251871	251882	01/04/1985: Spierlap, voorbereidende en bijkomende bewerking, per bewerking	01/04/1985 : Lambeau musculaire, par temps préparatoire et complémentaire, par temps
		01/04/2003: Spierlap, bijkomende bewerking, per tijd	01/04/2003 : Lambeau musculaire, temps complémentaire, par temps
251893	251904	Spierhuidlap	Lambeau musculo-cutané
251915	251926	Vrijmaken van enkelvoudige weefselflap (bv. Spier) en klaarmaken van de vaatsteel voor microchirurgische transfer	Prélèvement d'un lambeau mono-tissulaire (ex : musculaire), et préparation du pédicule en vue du transfert microchirurgical
251930	251941	Vrijmaken van samengestelde weefselflap (bv. osteo septo cutaan) en klaarmaken van de vaatsteel voor microchirurgische transfert	Prélèvement d'un lambeau composite pluri-tissulaire (ex : ostéo-septo-cutané), et préparation du pédicule en vue du transfert microchirurgical
251952	251963	Vrijmaken van perforatorflap (vb: DIEP of SGAP) en klaarmaken van de vaatsteel voor microchirurgisch transfert	Prélèvement d'un lambeau perforateur (ex : DIEP ou SGAP) et préparation du pédicule en vue du transfert microchirurgical
258930	258941	Modelleren en functionele adaptatie van een gesteeld of vrij microvasculair geanastomoseerd weefseltransplantaat	Modelage et adaptation fonctionnelle d'un transplant tissulaire pédiculé ou libre, avec anastomose microvasculaire
258952	258963	Modelleren en functionele adaptatie, door middel van osteotomie en osteosynthesemateriaal, van een vrij microvasculair geanastomoseerd	Modelage et adaptation fonctionnelle, par ostéotomie et matériel d'ostéosynthèse, d'un transplant tissulaire libre composé de plusieurs

Outpatient	Inpatient	Dutch Description	French Description
		uit meerdere weefsels bestaand weefseltransplantaat (weke delen en bot of kraakbeen)	tissus (parties molles et os ou cartilage), avec anastomose microvasculaire
311371	311382	Enkelvoudige osteotomie (inclusief afname) van been uit beendermassief van gelaat	Ostéotomie simple (prélèvement compris) d'un os du massif osseux de la face
312071	312082	Faryngoplastiek (type Sanvenero-Rosselli)	Pharyngoplastie (type Sanvenero-Rosselli)
312616	312620	Benige rekonstruktie in het maxillo-faciaal massief bij middel van een gesteelde osteo-myo-cutane lap, inclusief de ribresectie en osteosynthese (geschrapt op 01/5/2009)	Reconstruction osseuse dans le massif maxillo-facial au moyen d'un lambeau ostéo-myo-cutané pédiculé, y compris la résection costale et l'ostéo-synthèse (supprimé le 01/05/2009)
312631	312642	01/07/1986: Benige rekonstruktie in het maxillo-faciaal massief bij middel van een vrije osteo-myo-cutane lap met microchirurgisch hechten, inclusief de ribresectie en osteosynthese	01/07/1986 : Reconstruction osseuse dans le massif maxillo-facial au moyen d'un lambeau ostéo-myo-cutané libre avec suture micro-chirurgicale, y compris la résection costale et l'ostéosynthèse
		01/02/2004: Benige reconstruktie in het maxillo-faciaal massief bij middel van een vrije fascio-osteoperiostale of myo-osseuze of osseo-myo-cutane lap met microchirurgisch hechten, inclusief donorsitepreparatie en osteosynthese (geschrapt op 01/05/2009)	01/02/2004 : Reconstruction osseuse dans le massif maxillo-facial au moyen d'un lambeau libre fascio-ostéopériosté ou myo-osseux ou ostéo-myo-cutané avec suture micro-chirurgicale, y compris la préparation du site donneur et l'ostéosynthèse (supprimé le 01/05/2009)
312874	312885	Gesteelde huid- of mucosalapplastie, hoofdbewerking	Plastie à lambeau pédiculé cutané ou muqueux, temps principal
312896	312900	Gesteelde huid- of mucosalapplastie, bijkomende bewerking	Plastie à lambeau pédiculé cutané ou muqueux, temps complémentaire
313036	313040	Modelleren en functionele adaptatie van een gesteeld of vrij microvasculair geanastomoseerd weefseltransplantaat	Modelage et adaptation fonctionnelle d'un transplant tissulaire pédiculé ou libre, avec anastomose microvasculaire
313051	313062	Modelleren en functionele adaptatie, door middel van osteotomie en osteosynthesemateriaal, van een vrij microvasculair geanastomoseerd uit meerdere weefsels bestaand weefseltransplantaat (weke delen en bot of kraakbeen)	Modelage et adaptation fonctionnelle, par ostéotomie et matériel d'ostéosynthèse, d'un transplant tissulaire libre composé de plusieurs tissus (parties molles et os ou cartilage), avec anastomose microvasculaire
251296	251300	Over een oppervlakte van 10 cm² tot 50 cm²	Couvrant une surface de 10 cm² à 50 cm²
312933	312944	Preprothetische of oncologische gingivale of mucosale ent over een oppervlakte van > 5cm²	Greffe préprothétique ou greffe oncologique gingivale ou muqueuse couvrant une surface > 5 cm²

Appendix 3.3.   Nomenclature codes for radiotherapy

Appendix 3.3.1. Codes for radiotherapy with curative intent

Table 48 – Nomenclature codes for radiotherapy with curative intent

Outpatient	Inpatient	Dutch Description	French Description
External radiotherapy			
444135	444146	Forfaitair honorarium voor een eenvoudige uitwendige bestralingsreeks van minstens 11 tot 35 fracties voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 2	Honoraires forfaitaires pour une série d'irradiations externes simples de 11 à 35 fractions chez un patient qui répond aux critères ou pathologie repris en catégorie 2
444150	444161	Forfaitair honorarium voor een complexe uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 3	Honoraires forfaitaires pour une série d'irradiations externes complexes chez un patient qui répond aux critères ou pathologie repris en catégorie 3
444172	444183	Forfaitair honorarium voor een complexe uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 4	Honoraires forfaitaires pour une série d'irradiations externes complexes chez un patient qui répond aux critères ou pathologie repris en catégorie 4
Brachy radiotherapy			
444216	444220	Forfaitair honorarium voor exclusieve curietherapie voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 7	Honoraires forfaitaires pour curiethérapie exclusive chez un patient qui répond aux critères ou pathologie repris en catégorie 7
444253	444264	Forfaitair honorarium voor exclusieve curietherapie voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 8	Honoraires forfaitaires pour curiethérapie exclusive chez un patient qui répond aux critères ou pathologie repris en catégorie 8
External and brachy RT combined			
444290	444301	Forfaitair honorarium voor curietherapie gecombineerd met uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 5	Honoraires forfaitaires pour curiethérapie combinée à une série d'irradiations externes chez un patient qui répond aux critères ou pathologie repris en catégorie 5
444312	444323	Forfaitair honorarium voor curietherapie gecombineerd met uitwendige bestralingsreeks voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 6	Honoraires forfaitaires pour curiethérapie combinée à une série d'irradiations externes chez un patient qui répond aux critères ou pathologie repris en catégorie 6

Appendix 3.3.2. Codes for radiotherapy with palliative intent

Table 49 – Nomenclature codes for radiotherapy with palliative intent

Outpatient	Inpatient	Dutch Description	French Description
444113	444124	Forfaitair honorarium voor een eenvoudige uitwendige bestralingsreeks van 1 tot 10 fracties voor een patiënt die beantwoordt aan de criteria of lijdt aan een aandoening opgenomen in categorie 1	Honoraires forfaitaires pour une série d'irradiations externes simples de 1 à 10 fractions chez un patient qui répond aux critères ou pathologie repris en catégorie 1

Appendix 3.4. ICD-9-CM codes to define surgery in the MZG – RHM database

Table 50 – ICD-9-CM codes included to define surgery with curative intent for oral cavity in the MZG – RHM database

Number	Description
251	EXCISION OR DESTRUCTION OF LESION OR TISSUE OF TONGUE
252	PARTIAL GLOSSECTOMY
253	COMPLETE GLOSSECTOMY
254	RADICAL GLOSSECTOMY
2772	EXCISION OF UVULA
2731	LOCAL EXCISION OR DESTRUCTION OF LESION OR TISSUE OF BONY PALATE
2732	WIDE EXCISION OR DESTRUCTION OF LESION OR TISSUE OF BONY PALATE
2749	OTHER EXCISION OF MOUTH
2933	PHARYNGECTOMY (PARTIAL)
2939	OTHER EXCISION OR DESTRUCTION OF LESION OR TISSUE OF PHARYNX
7631	PARTIAL MANDIBULECTOMY
7639	PARTIAL OSTECTOMY OF OTHER FACIAL BONE
7641	TOTAL MANDIBULECTOMY WITH SYNCHRONOUS RECONSTRUCTION
7642	OTHER TOTAL MANDIBULECTOMY
7644	TOTAL OSTECTOMY OF OTHER FACIAL BONE WITH SYNCHRONOUS RECONSTRUCTION

7645	OTHER TOTAL OSTECTOMY OF OTHER FACIAL BONE

Table 51 – ICD-9-CM codes included to define surgery with curative intent for oropharynx in the MZG – RHM database

Number	Description
251	EXCISION OR DESTRUCTION OF LESION OR TISSUE OF TONGUE
252	PARTIAL GLOSSECTOMY
253	COMPLETE GLOSSECTOMY
254	RADICAL GLOSSECTOMY
2772	EXCISION OF UVULA
2731	LOCAL EXCISION OR DESTRUCTION OF LESION OR TISSUE OF BONY PALATE
2732	WIDE EXCISION OR DESTRUCTION OF LESION OR TISSUE OF BONY PALATE
2749	OTHER EXCISION OF MOUTH
2933	PHARYNGECTOMY (PARTIAL)
2939	OTHER EXCISION OR DESTRUCTION OF LESION OR TISSUE OF PHARYNX
3021	EPIGLOTTIDECTOMY (PARTIAL LARYNGECTOMY)
7631	PARTIAL MANDIBULECTOMY
7639	PARTIAL OSTECTOMY OF OTHER FACIAL BONE
7641	TOTAL MANDIBULECTOMY WITH SYNCHRONOUS RECONSTRUCTION
7642	OTHER TOTAL MANDIBULECTOMY
7644	TOTAL OSTECTOMY OF OTHER FACIAL BONE WITH SYNCHRONOUS RECONSTRUCTION
7645	OTHER TOTAL OSTECTOMY OF OTHER FACIAL BONE
282	TONSILLECTOMY WITHOUT ADENOIDECTOMY
283	TONSILLECTOMY WITH ADENOIDECTOMY
284	EXCISION OF TONSIL TAG
285	EXCISION OF LINGUAL TONSIL
286	ADENOIDECTOMY WITHOUT TONSILLECTOMY

Table 52 – ICD-9-CM codes included to define surgery with curative intent for hypopharynx in the MZG – RHM database

Number	Description
2933	PHARYNGECTOMY (PARTIAL)
2939	OTHER EXCISION OR DESTRUCTION OF LESION OR TISSUE OF PHARYNX
301	HEMILARYNGECTOMY
3021	EPIGLOTTIDECTOMY (PARTIAL LARYNGECTOMY)
3022	VOCAL CORDECTOMY (PARTIAL LARYNGECTOMY)
3029	OTHER PARTIAL LARYNGECTOMY (PARTIAL LARYNGECTOMY)
303	COMPLETE LARYNGECTOMY
304	RADICAL LARYNGECTOMY
3009	OTHER EXCISION OR DESTRUCTION OF LESION OR TISSUE OF LARYNX (stripping of vocal cords)
301	HEMILARYNGECTOMY
3021	EPIGLOTTIDECTOMY (PARTIAL LARYNGECTOMY)

Table 53 – ICD-9-CM codes included to define surgery with curative intent for larynx in the MZG – RHM database

Number	Description
301	HEMILARYNGECTOMY
3021	EPIGLOTTIDECTOMY (PARTIAL LARYNGECTOMY)
3022	VOCAL CORDECTOMY (PARTIAL LARYNGECTOMY)
3029	OTHER PARTIAL LARYNGECTOMY (PARTIAL LARYNGECTOMY)
303	COMPLETE LARYNGECTOMY
304	RADICAL LARYNGECTOMY
3009	OTHER EXCISION OR DESTRUCTION OF LESION OR TISSUE OF LARYNX (stripping of vocal cords)
301	HEMILARYNGECTOMY
3021	EPIGLOTTIDECTOMY (PARTIAL LARYNGECTOMY)

Appendix 3.5. ATC codes for systemic therapy

The Anatomical Therapeutic Chemical (ATC) Classification System is used for the classification of active ingredients of drugs according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties. Each bottom-level ATC code stands for a pharmaceutically used substance, or a combination of substances, in a single indication (or use).

- The first level of the code indicates the anatomical main group and consists of one letter (L=Antineoplastic and immunomodulating agents).

- The second level of the code indicates the therapeutic subgroup and consists of two digits.

- The third level of the code indicates the therapeutic/pharmacological subgroup and consists of one letter.

- The fourth level of the code indicates the chemical/therapeutic/pharmacological subgroup and consists of one letter.

- The fifth level of the code indicates the chemical substance and consists of two digits.

Appendix 3.5.1. ATC codes for chemotherapy

Table 54 – ATC codes for chemotherapy

ATC code	Description ATC-code
L01AA01	CYCLOPHOSPHAMIDE
L01AA06	IFOSFAMIDE
L01BA01	METHOTREXATE
L01BA03	RALTITREXED
L01BA04	PEMETREXED
L01BC02	FLUOROURACIL
L01BC05	GEMCITABINE
L01BC06	CAPECITABINE
L01CA01	VINBLASTINE

ATC code	Description ATC-code
L01CA02	VINCRISTINE
L01CA03	VINDESINE
L01CA04	VINORELBINE
L01CB01	ETOPOSIDE
L01CD01	PACLITAXEL
L01CD02	DOCETAXEL
L01DB01	DOXORUBICIN
L01DB03	EPIRUBICIN
L01DC01	BLEOMYCIN
L01DC03	MITOMYCIN
L01XA01	CISPLATIN
L01XA02	CARBOPLATIN
L01XX05	HYDROXYCARBAMIDE

Appendix 3.5.2. ATC codes for targeted therapy

Table 55 – ATC codes for targeted therapy

ATC code	Description ATC-code
L01XC06	CETUXIMAB
L01XE03	ERLOTINIB
L01XE10	EVEROLIMUS

APPENDIX 4. CASE MIX ADJUSTMENT

Table 56 – List of ICD-9-CM codes and weights used for the Romano-Charlson score

	Comorbidities	Romano-Charlson version ICD-9-CM codes [32]	Weights
1	Myocardial infarction	410 412	1
2	Congestive Heart failure	402.01 402.11 402.91 425 428 429.3	1
3	Peripheral vascular disease	440 441 442 443 447.1 785.4 38.13-38.14(P) 38.16(P) 38.18(P) 38.33-38.34(P) 38.36(P) 38.38(P) 38.43-38.44(P) 38.46(P) 38.48(P) 39.22-39.26(P) 39.29(P)	1
4	Cerebrovascular disease	362.34 430-436 437-437.1 437.9 438 781.4	1

	Comorbidities	Romano-Charlson version ICD-9-CM codes [32]	Weights
		784.3 997.0 38.12(P) 38.42(P)	
5	Dementia	290. 331-331.2	1
6	Chronic pulmonary disease	415.0 416.8-416.9 491-494 496	1
7	Rheumatologic disease	710 714 **725***	1
8	Peptic ulcer disease	531-534	1
9	Mild liver disease	571.2 571.5-571.6 571.8-571.9 **571.4***	1
10	Diabetes, without chronic complications	250.0-250.3	1
11	Diabetes with chronic complications	250.4-250.9	**2**
12	Hemiplegia or paraplegia	342 344	2
13	Renal disease	585-586 V42.0 V45.1 V56 39.27(P) 39.42(P) 39.93-39.95(P) 54.98(P)	2
14	Any malignancies, including leukaemia and lymphoma**	140-171 174-195 200-208 273.0	2

Comorbidities		Romano-Charlson version ICD-9-CM codes [32]	Weights
		273.3 V10.46 60.5(P) 62.4-62.41(P)	
15	Moderate or severe liver disease	572.2-572.4 456.0-456.2 39.1(P) 42.91(P)	3
16	Metastatic solid tumour	196-199	6
17	AIDS	042-044	6

* Codes added to better capture the comorbidity in the MZG – RHM database; ** Because only patients with unique tumours were selected for the study, no patient will present a comorbidity belonging to the category 'Any malignancies, including leukaemia and lymphoma'; (P) refers to procedures.

APPENDIX 5. VALIDATION

Appendix 5.1. List of hospitals participating in the validation study

Brussels-Capital Region:

- CHU Saint Pierre (Brussels)
- Hôpitaux Iris Sud (Brussels)

Flemish Region:

- UZ Leuven (Leuven)
- UZ Brussel (Brussels)
- Jessa Ziekenhuis (Hasselt)
- AZ Sint-Elisabeth (Zottegem)
- AZ Sint-Maarten (Mechelen)
- AZ Jan Palfijn (Gent)
- Sint Jozefskliniek (Izegem)
- VZW Imelda (Bonheiden)

Walloon Region:

- CH De Jolimont – Lobbes (Lobbes)
- CHU Sart Tilman (Liège)
- Centre De Santé Des Fagnes (Chimay)
- CHR Verviers (Verviers)
- CHR De Huy (Huy)
- Intercommunale Hospitalière Famenne Ardenne Condroz (IFAC, Marche-en-Famenne)

Appendix 5.2. Algorithm to assign patients to one treatment hospital

To define the 'treatment hospital', the hospital where the following procedures took place were taken into account:

- Surgery of the primary tumour with curative intent
- Radiotherapy
- Chemotherapy
- Multidisciplinary team meeting (MDT)

For surgery, MDT and radiotherapy and chemotherapy without surgery, only interventions within the time frame one month before until six months after the incidence date were taken into account. When the patient received surgery, neo-adjuvant treatment within the time frame one month before the incidence date until date of surgery was taken into account and adjuvant treatment until six months after surgery was taken into account. If more than one intervention was found within the time frame, only the closest to the incidence date (or surgery date in case of adjuvant treatment) was retained.

The following rules were respected to define one 'treatment hospital' per tumour. The order in which they are stated hereafter, indicates the priority between the rules (1 = highest priority; 6 = lowest priority).

Priority rule (Cumulative percentage assigned patients per rule)

1) If only one centre was known, this centre was selected (64%)

2) Otherwise, if there was surgery of the primary tumour with curative intent, the centre of surgery was selected (78%)

3) Otherwise, if there was chemoradiotherapy, different options were possible:

    3a. If the centre of chemo was the same as the centre of RT, this centre was selected (82%)

    3b. If the centre of chemo was the same as the centre of MDT, this centre was selected (90%)

    3c. If the centre of RT was the same as the centre of MDT, this centre was selected (90%)

    3d. Else the centre of chemo was selected (93%)

    3e. If the centre could not be determined based on the above-mentioned rules, the centre of RT was selected (93%)

4) Otherwise, if there was radiotherapy only, the centre of RT was selected (98%)

5) Otherwise, if there was chemotherapy only, the centre of chemo was selected (100%)

Appendix 5.3. Information provided to the hospitals for each assigned patient and checks asked to be done

- Patient identifiers: Social Security Identification Number (INSZ – NISS), a coded patient ID
- Patient characteristics: performance status at time of diagnosis (WHO-score)
- Tumour characteristics: incidence date, anatomic site (oral cavity, oropharynx, hypopharynx or larynx), topography, morphology, clinical stage (T, N and M), pathological stage (T, N and M)
- Diagnostic and staging procedures: multidisciplinary team meeting (MDT), MRI primary tumour, CT-scan primary tumour, biopsy primary tumour and cytology primary tumour
- Surgical procedures: surgery with curative intent of the primary tumour, lymphadenectomy and reconstructive surgery
- Radiotherapy/chemotherapy: radiotherapy/chemotherapy without surgery with curative intent, before surgery with curative intent, after surgery with curative intent

- Information on the rule used to assign the patient to the treatment hospital

For all diagnostic and therapeutic procedures, the date of the procedure according to IMA – AIM data was provided, as well as a variable indicating whether the procedure was performed within a defined time frame around the incidence date (or date of surgery if applicable) or not.

Hospitals were asked to perform the following tasks:

1. Verify the patient list: were these patients taken care of in your hospital for the defined cancer type?
2. Add those HNSCC patients diagnosed in 2013 who were incorrectly not assigned to your hospital;
3. Check for the complete patient list whether all information provided is correct.

Appendix 5.4. Validation of the algorithm to assign patients to one treatment hospital – results

The correctness and completeness of the patient lists (incidence year 2013) by hospital is presented in Figure 24. For the sixteen hospitals together, seven patients (1.8%) had to be excluded from the study:

- Two patients because they had a recurrence instead of a new cancer diagnosis;

- Two patients because they had a small larynx tumour (and only T3,4 should be included);

- Two patients because the primary localisation of their tumour was unknown;

- One patient because the tumour was not a squamous cell carcinoma.

- Additionally, for the sixteen hospitals together, six patients (1.6%) were excluded from the hospital lists as the assignment to the hospital was not correct; yet they were correctly included in the study:

- Four patients were not assigned to the correct hospital because the nomenclature code that was used to bill the surgical procedure was unspecific and was not included in the selection made for this study;

- Two patients were assigned to the centre of the main radiation oncology department instead of the centre of the satellite radiotherapy unit where the radiation took place.

Ten patients (2.6%) were added by the hospitals to their patient lists:

- One patient with a HNSCC was previously not reported in the BCR database;

- Four patients were incorrectly assigned to another hospital because the correct treatment scheme was not captured by the nomenclature selections that were used;

- Two patients with a HNSCC were recorded in the BCR database as a recurrence instead of a new diagnosis;

- One patient with a HNSCC was recorded in the BCR database as having an in situ tumour instead of an invasive one;

- One patient with a HNSCC was recorded in the BCR database as having a small hypopharynx tumour instead of an oropharynx tumour and was therefore excluded from the patient list;

- For one patient no IMA – AIM data were available and therefore this patient was not included in the validation study.

Figure 24 – Correctness and completeness of the patient lists (incidence year 2013) by hospital
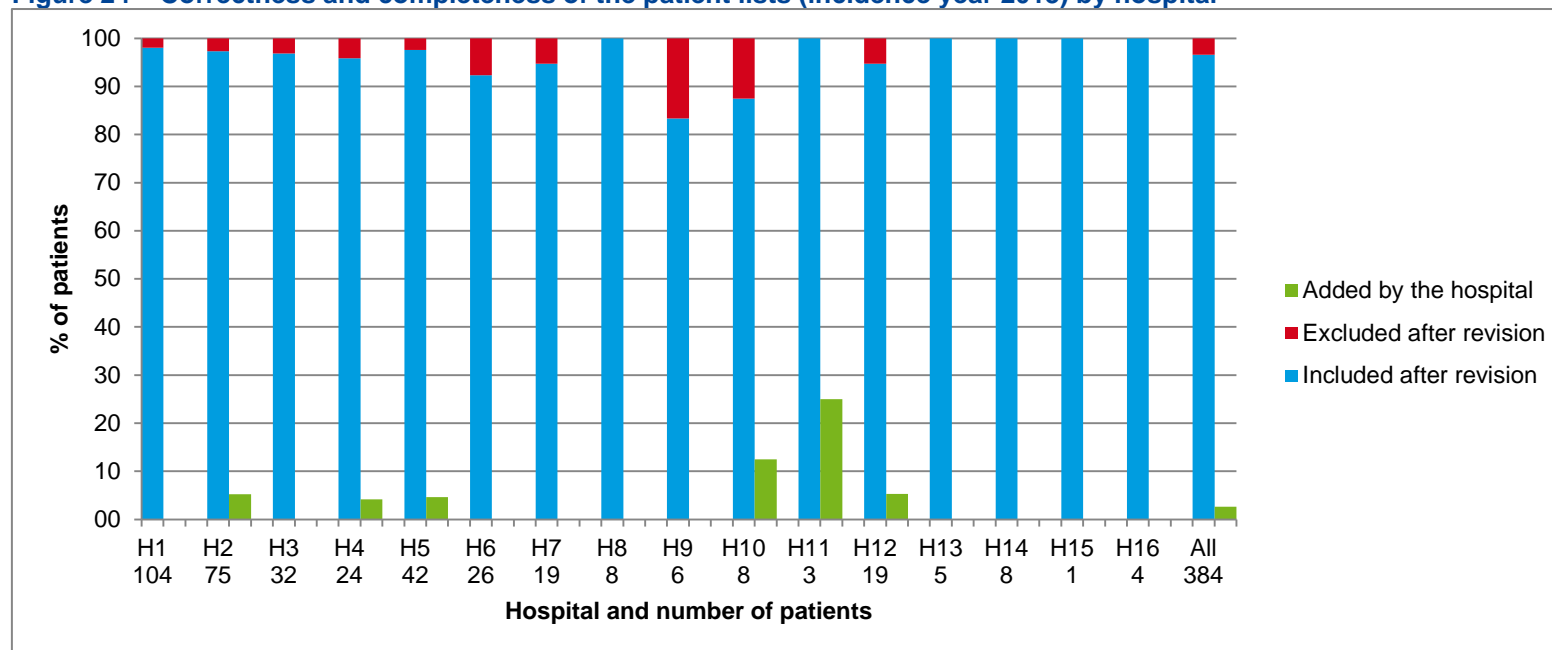
Note: One low-volume hospital was unable to look for additional patients.
Source: BCR – IMA

Table 57 – New algorithm to assign patients to one treatment hospital

Priority rule		Cumulative percentage of patients assigned (%)
1.	If only one centre was known (for surgery, radiotherapy, systemic therapy and/or MDT), this centre was selected	64
2.	Otherwise, if there was surgery of the primary tumour with curative intent, the centre of surgery was selected	78
3.	Otherwise, if there was (chemo)radiotherapy, the centre of radiotherapy was selected	98
4.	Otherwise, if there was systemic therapy only, the centre of systemic treatment was selected	100
5.	Otherwise (no primary treatment and no MDT), the centre of biopsy was selected	100

Appendix 5.5. Validation of patient and tumour characteristics as identified in the health insurance data linked to cancer registry data

Incidence date

The incidence date of the tumour is the date of first microscopic confirmation of the malignancy, and, if not available, it is the date of the technical or clinical investigation leading to the cancer diagnosis. For 96.8% of the tumours included in the validation process the incidence date as reported by the BCR was confirmed by the hospitals (Table 58). For nineteen tumours the incidence date was incorrect, but for only six of those nineteen the difference was larger than fourteen days. Small deviations of one or two days (which could be explained by the difference between the date of a surgical procedure (biopsy or resection) and the date of the pathology report of the specimen) were not taken into account.

Table 58 – Correctness of the incidence date of the tumour

	Number of patients	Proportion (%)
Total	**602**	**100.0**
Confirmed	**583**	**96.8**
Incorrect	**19**	**3.2**
≤ 14 days later than BCR	11	1.8
> 14 days later than BCR	4	0.7
≤ 14 days earlier than BCR	2	0.2
> 14 days earlier than BCR	2	0.2

Topography and anatomic site

For nine patients, the topography recorded in the linked database was corrected by the hospital into a topography leading to categorization of the tumour in another anatomic site, inside (N=6) or outside (N=3) the head and neck region (Table 59). Additionally, for 28 tumours the topography was changed without an influence on the anatomic site (e.g. a different topography within the oral cavity without an impact on the results of the validation study).

Table 59 – Correctness of anatomic site

	Number of patients	Proportion (%)
Total	**602**	**100.0**
Confirmed	**593**	**98.5**
Incorrect	**9**	**1.5**
• Oral cavity → Oropharynx	2	0.3
• Oral cavity → Lip	1	0.2
• Oral cavity → Unknown primary (C80.9)	1	0.2
• Oropharynx → Unknown primary (C80.9)	1	0.2
• Oropharynx → Hypopharynx (large tumour size)	1	0.2
• Oropharynx → Larynx (small tumour size)	2	0.3
• Oropharynx → Other than head and neck cancer	1	0.2

Morphology

The morphology of the tumour was indicated by the hospitals as incorrect in seven cases (1.2%): six times it was changed to another morphology within the selection of squamous cell carcinoma under study (no influence on the results of the study), and in one case outside this selection (this tumour should have been excluded from the study).

Clinical stage

The complete clinical T, N and M of 550 (91.4%) of the tumours was confirmed by the hospitals (Table 60). The majority of the changes made by the hospitals were in fact completion of missing information (25 times for clinical T, 26 times for clinical N and 8 times for clinical M) and should therefore be interpreted as incomplete data, rather than incorrect data.

For ten tumours the change of the clinical T concerned a switch between a small tumour (T1 or T2) and a large tumour (T3 or T4), with an impact on

the identification of 'surgery with curative intent' (see section 3.3.2). A negative lymph node status was three times corrected to positive lymph nodes. Distant metastases were two times incorrectly registered in the BCR database, where in fact there were no distant metastasis found based on clinical investigation.

Table 60 – Correctness of clinical stage

	Number of patients	Proportion (%)
Total	**602**	**100.0**
Confirmed clinical TNM	**550**	**91.4**
Incorrect clinical T	**37**	**6.1**
small → large	7	1.2
large → small	3	1.3
x → small	12	2.0
x → large	13	2.2
large → large	2	0.3
Incorrect clinical N	**29**	**4.8**
- → +	3	0.5
x → -	14	2.3
x → +	12	2.0
Incorrect clinical M	**11**	**1.8**
0 → x	1	0.2
+ → -	2	0.3
x → -	7	1.2
x → +	1	0.2

Pathological stage

Since 'surgery with curative intent' was not yet definitely defined at the time of the validation, it is impossible to report the number of patients for whom the pathological stage should be reported. Therefore, correctness of the pathological stage is reported with the total number of patients included in the validation as the denominator.

Hospitals reported changes in the pathological T, N and/or M categories for fourteen patients (2.3%) (Table 61). However, only few changes had a potential impact on the study (e.g. switch between small and large tumours). In line with the results of the clinical stage, changes often concerned the completion of missing information (four times for the pathological T and four times for the pathological N).

Table 61 – Correctness of pathological stage

	Number of patients	Proportion (%)
Total	**602**	**100.0**
Confirmed pathological TNM	**588**	**97.7**
Incorrect pathological T	**8**	**1.3**
small ➔ large	2	0.3
x ➔ small	2	0.3
x ➔ large	2	0.3
large ➔ x	1	0.2
large ➔ large	1	0.2
Incorrect pathological N	**6**	**1.0**
- ➔ x	2	0.3
x ➔ -	1	0.2
x ➔ +	3	0.5

Appendix 5.6. Validation of diagnostic and therapeutic procedures as identified in the health insurance data linked to cancer registry data

For this purpose the same patient list was used as described in section 3.5.3. The results are presented for each procedure on two levels:

1. **Only taking into account those patients correctly assigned to the hospitals (N=576), evaluating the concordance between BCR and hospital data**

   Results are reported by anatomic site: (a) correct positive: the total number of patients for whom the procedure was identified within the predefined time frame around the incidence date (or the date of surgery if applicable) by the BCR and the hospitals, (b) false positive: only identified by the BCR, (c) false negative: only identified by the hospitals, and (d) correct negative: identified by neither the BCR nor the hospitals.

2. **Taking into account all patients on the lists as assigned to the hospitals by the BCR (N=602) versus the patients correctly assigned to the hospitals (N=576), evaluating the concordance between the proportions**

   An overview is given of the proportion of patients for whom the procedure was identified within the defined time frame as provided by the BCR, compared with the proportion of patients for whom the procedure was reported (within the same time frame) by the hospital. The overall percentage of change (for the sixteen hospitals together) between both proportions is presented to discover the difference in results on a national level when using different data sources (health insurance data linked to the cancer registry versus hospital data) for the calculation of quality indicators of care. Ranges of the percentage of change are also presented by anatomic site and aggregated for high/medium volume hospitals versus low-volume hospitals to discover the difference in results on the hospital level. It should be noted that changes in the data for a small number of patients can cause large deviations in (proportional) results for low-volume hospitals. Therefore,

the results of the low-volume hospitals should be interpreted with caution.

Multidisciplinary team meeting (MDT) within six months after incidence date

For the patients correctly assigned to the hospitals, the MDT was in 95% of the cases correctly defined by the BCR (Appendix 5.6, Table 62). For SCC

of the oral cavity this was lower than for the other anatomic sites (92%, i.e. 69% + 23%). Except for one case, all errors were due to missing information on MDTs in the IMA – AIM database caused by billing rules. For example, the number of reimbursed MDT's is limited to maximum one per year, so in reality patients may have been discussed multiple times during an MDT, but only one can be attested. This attested MDT (registered in the IMA – AIM database) may well fall outside the defined time frame and hence not selected by the BCR.

Table 62 – Patients discussed during a multidisciplinary team meeting (MDT): concordance between health insurance data linked to cancer registry data (BCR) and the hospitals' data (Hospital)

| | Number of patients confirmed as correctly assigned to the sixteen hospitals | Number of patients discussed during MDT according to … (%) | | | | | | | |
| | | BCR and Hospital (true positive) | | BCR only (false positive) | | Hospital only (false negative) | | None (true negative) | |
Anatomic site	N	N	%	N	%	N	%	N	%
Oral cavity	213	146	69	1	0	17	8	49	23
Oropharynx	217	185	85	0	0	8	4	24	11
Hypopharynx	55	46	84	0	0	2	4	7	13
Larynx	91	78	86	0	0	2	2	11	12
Total	576	455	79	1	0	29	5	91	16

When the proportion of patients discussed during an MDT based on available data for the BCR was compared to the proportion based on hospital data, the proportion was, in general, 5% underestimated using administrative IMA – AIM data (Table 63), with a larger error (8%) for SCC of the oral cavity. There is a large variation between the ranges of this difference between the hospitals, especially in low-volume hospitals.

Table 63 – Patients discussed during a multidisciplinary team meeting (MDT): results using health insurance data linked to cancer registry data (BCR) versus hospital data (Hospital)

	% of patients discussed during MDT according to…		% of change	Range % of change	
	BCR	Hospital	Overall	High/medium volume hospital	Low-volume hospital
Anatomic site					
Oral cavity	68	76	8	[0,+30]	[-50,+17]
Oropharynx	86	89	3	[0,+13]	[-17,+17]
Hypopharynx	85	87	2	[-3,+14]	[0,0]
Larynx	86	87	1	[0,+13]	[0,0]
Total	79	84	5	[+1,+12]	[-3,+6]

MRI of the primary tumour within three months around incidence date

For the patients correctly assigned to the hospitals, the use of an MRI for the primary tumour was in 95% of the cases correctly defined by the BCR (Table 64). For SCC of the oral cavity (94%) and the oropharynx (93%) the proportions were somewhat lower than for the other anatomic sites.

The observed discordance between data had various reasons. The most important reason (N=21) for an underestimation, especially observed for SCC of the oral cavity and oropharynx, was that the nomenclature code (459395/459406) was not included in the selection of the BCR to identify MRI, because this code can also be used for an MRI to search for metastases (N=21). The other reason for erroneously not selecting the MRI was an administrative error (N=3). Six times an MRI was erroneously selected by the BCR because the MRI was performed in another hospital without certainty about the intent (N=1), was not performed for the primary tumour (N=3) or was performed for another tumour (N=3).

Table 64 – Patients with an MRI of the primary tumour: concordance between health insurance data linked to cancer registry data (BCR) and the hospitals' data (Hospital)

| | Number of patients confirmed as correctly assigned to the sixteen hospitals | Number of patients with an MRI of the primary tumour according to … (%) | | | | | | | |
| | | BCR and Hospital (true positive) | | BCR only (false positive) | | Hospital only (false negative) | | None (true negative) | |
Anatomic site	N	N	%	N	%	N	%	N	%
Oral cavity	213	49	23	3	1	10	5	151	71
Oropharynx	217	55	25	2	1	12	6	148	68
Hypopharynx	55	11	20	1	2	1	2	42	76
Larynx	91	11	12	0	0	1	1	79	87
Total	576	126	22	6	1	24	4	420	73

When the proportion of patients with an MRI of the primary tumour based on available data for the BCR was compared to the proportion based on hospital data, the proportion was, in general, 4% underestimated using administrative IMA – AIM data (Table 65), with a larger error (10%) for SCC of the oropharynx. There is a large variation between the ranges of this difference between the hospitals, in high/medium volume hospitals as well as in low-volume hospitals.

Table 65 – Patients with an MRI of the primary tumour: results using health insurance data linked to cancer registry data (BCR) versus hospital data (Hospital)

| | % of patients undergoing an MRI of the primary tumour | | % of change | Range % of change | |
	BCR	Hospital	Overall	High/medium volume hospital	Low-volume hospital
Anatomic site					
Oral cavity	25	29	3	[-13,+29]	[-50,+8]
Oropharynx	26	36	10	[-3,+45]	[-17,+3]
Hypopharynx	20	22	2	[-1,+14]	[0,0]
Larynx	12	13	1	[-8,+5]	[0,0]
Total	23	27	4	[-4,+30]	[-6,+6]

CT-scan of the primary tumour within three months around incidence date

For the patients correctly assigned to the hospitals, the use of a CT-scan for the primary tumour was in 99% of the cases correctly defined by the BCR (Table 66). All six errors were false negative cases for SCC of the oral cavity (N=5) and the oropharynx (N=1). Discordance between data was due to an error in the incidence date (N=1), a nomenclature code (458673/458684) that was not included in the selection by the BCR (N=2), the time frame of three months around the incidence date that was too short to capture the CT-scan (N=1), or due to administrative errors (e.g. incorrect date, misclassification; N=2).

Table 66 – Patients with a CT-scan of the primary tumour: concordance between health insurance data linked to cancer registry data (BCR) and the hospitals' data (Hospital)

	Number of patients confirmed as correctly assigned to the sixteen hospitals	Number of patients with a CT-scan of the primary tumour according to … (%)							
		BCR and Hospital (true positive)		BCR only (false positive)		Hospital only (false negative)		None (true negative)	
Anatomic site	**N**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Oral cavity	213	187	88	0	0	5	2	21	10
Oropharynx	217	208	96	0	0	1	0	8	4
Hypopharynx	55	54	98	0	0	0	0	1	2
Larynx	91	90	99	0	0	0	0	1	1
Total	576	539	94	0	0	6	1	31	5

When the proportion of patients with a CT-scan of the primary tumour based on available data for the BCR is compared to the proportion based on hospital data, the proportion was almost identical (Table 67). Except for SCC of the oral cavity, the percentage of change between both proportions was very low and there was little variation between the hospitals.

Table 67 – Patients with a CT-scan of the primary tumour: results using health insurance data linked to cancer registry data (BCR) versus hospital data (Hospital)

	% of patients undergoing a CT-scan		% of change	Range % of change	
	BCR	Hospital	Overall	High/medium volume hospital	Low-volume hospital
Anatomic site					
Oral cavity	88	90	2	[-2,+11]	[-17,+9]
Oropharynx	96	96	0	[-4,+2]	[0,0]
Hypopharynx	98	98	0	[0,0]	[0,0]
Larynx	99	99	0	[0,0]	[0,0]
Total	94	94	1	[0,+4]	[-3,+6]

Biopsy of the primary tumour within three months around incidence date

For the patients correctly assigned to the hospitals, a biopsy of the primary tumour was in 98% of the cases correctly defined by the BCR (Table 68). Errors occurred somewhat more for oropharynx and larynx, but were still limited. In eight cases a biopsy of the primary tumour was incorrectly selected by the BCR: in two cases a curative surgery was erroneously selected as a biopsy, in one case it concerned a biopsy of a metastasis, in three cases it concerned a biopsy of another tumour, in one case the error was due to an administrative error, and in a last case the biopsy was performed in another hospital for a non-oncological reason. A biopsy of the primary tumour was once missed by the BCR because of an incorrect incidence date registered in the cancer registry database and once because no single nomenclature code for a biopsy was identified in the IMA – AIM data (administrative error/misclassification).

Table 68 – Patients with a biopsy of the primary tumour: concordance between health insurance data linked to cancer registry data (BCR) and the hospitals' data (Hospital)

| | Number of patients confirmed as correctly assigned to the sixteen hospitals | Number of patients with a biopsy of the primary tumour according to … (%) | | | | | | | |
| | | BCR and Hospital (true positive) | | BCR only (false positive) | | Hospital only (false negative) | | None (true negative) | |
Anatomic site	N	N	%	N	%	N	%	N	%
Oral cavity	213	211	99	0	0	1	0	1	0
Oropharynx	217	212	98	4	2	1	0	0	0
Hypopharynx	55	54	98	1	2	0	0	0	0
Larynx	91	88	97	3	3	0	0	0	0
Total	576	565	98	8	1	2	0	1	0

When the proportion of patients with a biopsy of the primary tumour based on available data for the BCR is compared to the proportion based on hospital data, the proportion was, in general, about 1% overestimated using administrative IMA – AIM data, with no remarkable differences between anatomical sites (Table 69). Variation between hospitals was limited, but was higher in high/medium volume hospitals for SCC of the larynx and in low-volume hospitals for SCC of the oral cavity.

Table 69 – Patients with a biopsy of the primary tumour: results using health insurance data linked to cancer registry data (BCR) versus hospital data (Hospital)

| | % of patients with a biopsy of the primary tumour | | % of change | Range % of change | |
	BCR	Hospital	Overall	High/medium volume hospital	Low-volume hospital
Anatomic site					
Oral cavity	99	99	0	[0,0]	[-17,17]
Oropharynx	100	98	-1	[-8,+2]	[0,0]
Hypopharynx	100	98	-2	[-9,0]	[0,0]
Larynx	100	97	-3	[-14,0]	[0,0]
Total	100	98	-1	[-7,+1]	[-6,+6]

Cytology of the primary tumour within three months around incidence date

For the patients correctly assigned to the hospitals, cytology of the primary tumour was in 97% of the cases correctly defined by the BCR (Table 70), with almost no variation between the different anatomic sites. For sixteen cases the BCR selected incorrectly a cytology. Different reasons for these errors were a cytology for another tumour (N=7), cytology of a metastasis (N=3), or in six cases the cytology was performed for another (non-oncologic) reason. In one case the BCR missed the cytology because it was not registered in the IMA – AIM data (administrative error).

Table 70 – Patients with cytology: concordance between health insurance data linked to cancer registry data (BCR) and the hospitals' data (Hospital)

	Number of patients confirmed as correctly assigned to the sixteen hospitals	Number of patients with cytology according to … (%)						
		BCR and Hospital (true positive)		BCR only (false positive)		Hospital only (false negative)		None (true negative)	
Anatomic site	N	N	%	N	%	N	%	N	%
Oral cavity	213	33	15	4	2	0	0	176	83
Oropharynx	217	45	21	7	3	0	0	165	76
Hypopharynx	55	18	33	1	2	0	0	36	65
Larynx	91	15	16	4	4	1	1	71	78
Total	576	111	19	16	3	1	0	448	78

When the proportion of patients with cytology based on available data for the BCR is compared to the proportion based on hospital data, the proportion was, in general, 3% overestimated using administrative IMA – AIM data (Table 71), with the highest errors (5%) for SCC of the oropharynx.

Although the difference between the two proportions seemed acceptable, large variations in the percentage of change between high/medium volume hospitals as well as low-volume hospitals were observed.

Table 71 – Patients with cytology: results using health insurance data linked to cancer registry data (BCR) versus hospital data (Hospital)

	% of patients with cytology		% of change	Range % of change	
	BCR	Hospital	Overall	High/medium volume hospital	Low-volume hospital
Anatomic site					
Oral cavity	17	15	-2	[-8,+4]	[-50,+19]
Oropharynx	24	20	-3	[-10,+1]	[-17,+4]
Hypopharynx	38	33	-5	[-21,0]	[0,0]
Larynx	18	16	-2	[-13,+25]	[0,0]
Total	22	19	-3	[-7,+1]	[-6, +10]

Surgery with curative intent for the primary tumour within six months after incidence date

For the patients correctly assigned to the hospitals, surgery with curative intent for the primary tumour was in 96% of the cases correctly defined by the BCR (Table 72). The concordance between data was the lowest in SCC of the oral cavity (94%) and highest for the larynx (limited to large tumours (T3,4)) (98%). For SCC of the oral cavity and of the oropharynx errors concerned most often false positive cases, where the BCR incorrectly selected a procedure in the IMA – AIM data as a surgery with curative intent.

For SCC of the oral cavity these errors were due to the selection of nomenclature codes 311312/311323, 310914/310925, 353231/353242 and 310590/310601, which were apparently used for diagnostic purposes (N=9). Other reasons for false positive results were: one case where only a lymphadenectomy was performed and one case where the surgery did not concern the primary tumour (N=1). In one case with SCC of the oral cavity the BCR missed the surgery because it was registered in the IMA – AIM data with a nomenclature code (258075/258086) that was not selected for the study. Additionally to the results presented in Table 72, a wrong date for the surgical procedure with curative intent was selected for sixteen SCC of the oral cavity. In those cases the selected date was in fact the date of a

diagnostic procedure, while the surgery with curative intent took place on a later date. The nomenclature codes 220312/220323, 220334/220345, 310590/310601, 310914/310925, 310951/310926, 311135/311146, 353231/353242 were used in those cases.

For oropharynx the BCR erroneously selected surgery with curative intent because only a lymphadenectomy took place during the procedure (N=3), it concerned a diagnostic procedure (N=2), the surgery was performed with palliative intent (N=1) and in another case an incorrect topography was registered in the cancer registry database and thus a nomenclature code not applicable for the correct anatomic site was used.

Only two errors were found for large tumours (T3,4) of the hypopharynx, both false negative: once because the nomenclature code (258090/258101) used in the IMA – AIM data was not included in the selection for the project and once because the defined time frame around the incidence date was too narrow to capture the procedure.

For large tumours (T3,4) of the larynx a nomenclature code (258090/258101) not included in the selection for the project was once the reason for missing a surgery with curative intent by the BCR. Once the BCR incorrectly selected a surgery of the primary tumour, while in fact the procedure only concerned a lymphadenectomy.

Table 72 – Patients undergoing surgery with curative intent: concordance between health insurance data linked to cancer registry data (BCR) and the hospitals' data (Hospital)

| | Number of patients confirmed as correctly assigned to the sixteen hospitals | Number of patients undergoing surgery with curative intent according to … (%) | | | | | | | |
| | | BCR and Hospital (true positive) | | BCR only (false positive) | | Hospital only (false negative) | | None (true negative) | |
Anatomic site	N	N	%	N	%	N	%	N	%
Oral cavity	213	150	70	10	5	1	0	52	24
Oropharynx	217	49	23	7	3	0	0	161	74
Hypopharynx	55	9	16	0	0	2	4	44	80
Larynx	91	39	43	1	1	1	1	50	55
Total	576	247	43	18	3	4	1	307	53

When the proportion of patients undergoing surgery with curative intent for the primary tumour based on available data for the BCR is compared to the proportion based on hospital data, in general, the proportion was almost identical (Table 73): a small overestimation for SCC of the oral cavity and oropharynx and a small underestimation for SCC of the hypopharynx. For SCC of the larynx the proportions were identical. There was a large variation between hospitals, especially in low-volume hospitals, where changes in small numbers have an enormous impact on the proportions.

Table 73 – Patients undergoing surgery with curative intent: results using health insurance data linked to cancer registry data (BCR) versus hospital data (Hospital)

| | % of patients undergoing surgery with curative intent | | % of change | Range % of change | |
	BCR	Hospital	Overall	High/medium volume hospital	Low-volume hospital
Anatomic site					
Oral cavity	74	71	-3	[-10,8]	[-33,17]
Oropharynx	25	23	-2	[-13,2]	[-28,6]
Hypopharynx	18	20	2	[-10,3]	[0,100]
Larynx	44	44	0	[-8,0]	[-20,100]
Total	46	44	-2	[-8,2]	[-13,9]

Lymphadenectomy within six months after incidence date

For the patients correctly assigned to the hospitals, a lymphadenectomy was in almost 100% of the cases correctly defined by the BCR (Table 74), except for one case where the BCR missed the procedure because it was not registered in the IMA – AIM database (administrative error).

Table 74 – Patients undergoing lymphadenectomy: concordance between health insurance data linked to cancer registry data (BCR) and the hospitals' data (Hospital)

| | Number of patients confirmed as correctly assigned to the sixteen hospitals | Number of patients undergoing lymphadenectomy according to … (%) | | | | | | | |
| | | BCR and Hospital (true positive) | | BCR only (false positive) | | Hospital only (false negative) | | None (true negative) | |
Anatomic site	N	N	%	N	%	N	%	N	%
Oral cavity	213	115	54	0	0	1	0	97	46
Oropharynx	217	45	21	0	0	0	0	172	79
Hypopharynx	55	9	16	0	0	0	0	46	84
Larynx	91	38	42	0	0	0	0	53	58
Total	576	207	36	0	0	1	0	368	64

When the proportion of patients undergoing a lymphadenectomy based on available data for the BCR is compared to the proportion based on hospital data, in general, these proportions were found to be quite stable (Table 75). Changes between the proportions were predominantly caused by changes in the denominators. Variation between hospitals was large in low-volume hospitals.

Table 75 – Patients undergoing lymphadenectomy: results using health insurance data linked to cancer registry data (BCR) versus hospital data (Hospital)

	% of patients undergoing LND		% of change	Range % of change	
	BCR	Hospital	Overall	High/medium volume hospital	Low-volume hospital
Anatomic site					
Oral cavity	54	54	1	[-4,+5]	[-50,+17]
Oropharynx	21	21	0	[-3,+2]	[-33,+17]
Hypopharynx	18	16	-1	[-10,+3]	[0,0]
Larynx	42	42	0	[-8,0]	[0,0]
Total	36	36	0	[-2,+2]	[-12,+8]

Reconstructive surgery within six months after incidence date

For the patients correctly assigned to the hospitals, reconstructive surgery was in almost 100% of the cases correctly defined by the BCR (Table 76), except in four cases. The BCR missed the procedure three times because it was not registered in the IMA – AIM database. One time a reconstructive surgery was erroneously selected by the BCR due to the use of an incorrect nomenclature code for another procedure in the IMA – AIM data.

Table 76 – Patients undergoing reconstructive surgery: concordance between health insurance data linked to cancer registry data (BCR) and the hospitals' data (Hospital)

	Number of patients confirmed as correctly assigned to the sixteen hospitals	Number of patients undergoing reconstructive surgery according to … (%)							
		BCR and Hospital (true positive)		BCR only (false positive)		Hospital only (false negative)		None (true negative)	
Anatomic site	N	N	%	N	%	N	%	N	%
Oral cavity	213	83	39	1	0	1	0	128	60
Oropharynx	217	9	4	0	0	0	0	208	96
Hypopharynx	55	3	5	0	0	0	0	52	95
Larynx	91	7	8	0	0	2	2	82	90
Total	576	102	18	1	0	3	1	470	82

When the proportion of patients undergoing reconstructive surgery based on available data for the BCR is compared to the proportion based on hospital data, in general, these proportions were found to be quite stable (Table 77). Changes between the proportions were predominantly caused by changes in the denominators. Variation between hospitals was especially seen in low-volume hospitals and most pronounced for the oral cavity.

Table 77 – Patients undergoing reconstructive surgery: results using health insurance data linked to cancer registry data (BCR) versus hospital data (Hospital)

| | % of patients undergoing reconstructive surgery | | % of change | Range % of change | |
	BCR	Hospital	Overall	High/medium volume hospital	Low-volume hospital
Anatomic site					
Oral cavity	41	41	0	[-6,+3]	[-50,+17]
Oropharynx	4	4	0	[0,1]	[0,2]
Hypopharynx	7	6	-2	[-10,1]	[0,0]
Larynx	7	10	3	[0,+25]	[0,0]
Total	19	19	0	[-2,+3]	[-9,+8]

Radiotherapy within six months after incidence date/before or six months after date of surgery with curative intent

In total, twenty errors were observed for radiotherapy for all anatomic sites. Ten errors were due to an error in the identification of surgery with curative intent. Another six errors were programming errors which could be corrected for the main study. Two radiotherapy series were not found in the IMA – AIM data (administrative errors/misclassifications) and another two series turned out to be palliative.

Because RT is billed at the end date of the series, the start date is not always mentioned in the IMA – AIM database. For those cases, the Belgian Cancer

Registry developed an algorithm to estimate the start date. In 51 cases, the start date defined by the BCR did not perfectly correspond to the start date as reported by the hospitals. However, only in six cases the difference between the estimated start date and the real start date was larger than fourteen days.

Chemotherapy within six months after incidence date/before or six months after date of surgery with curative intent

For chemotherapy, eighteen errors were observed for all anatomic sites. Eleven errors were due to an error for surgery with curative intent. Another error occurred because the patient received neo-adjuvant chemotherapy before chemoradiotherapy, which is a treatment scheme that cannot be deduced from the IMA – AIM data (cf. section 3.3.2). Two times chemotherapy was considered as adjuvant treatment by the BCR, but was in reality given with palliative intent, twice the reason for erroneously selecting chemotherapy was unknown. One time the hospital reported that Celecoxib was administered, and in another patient Purinethol. However in the analyses of the quality indicators, both products were not considered chemotherapy applicable for HNSCC.

APPENDIX 6.   DESCRIPTIVE DATA

Appendix 6.1.   Patient and tumour characteristics

Table 78 – Patient characteristics at time of diagnosis (HNSCC, incidence 2009-2014)

	Total (N=9 245)		Oral cavity (N=2 665)		Oropharynx (N=2 745)		Hypopharynx (N=1 137)		Larynx (N=2 698)	
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**
Gender										
Male	7 017	75.9	1 770	66.4	1 998	72.8	974	85.7	2 275	84.3
Female	2 228	24.1	895	33.6	747	27.2	163	14.3	423	14.3
Age group										
Mean, SD (years)	62.3	SD11.1	62.2	SD12.4	60.8	SD10.1	61.4	SD9.5	64.3	SD10.8
Median, Range (years)	61.0	19 - 105	61.0	19 - 105	60.0	19 - 102	61.0	33 - 94	64.0	19 - 98
<50 years	930	10.1	339	12.7	319	11.6	84	7.4	188	7.0
50-59 years	3 058	33.1	869	32.6	1 013	36.9	437	38.4	739	27.4
60-69 years	3 047	33.0	772	29.0	916	33.4	411	36.2	948	35.1
70-79 years	1 481	16.0	410	15.4	364	13.3	146	12.8	561	20.8
80+ years	729	7.9	275	10.3	133	4.9	59	5.2	262	9.7
WHO performance status										
0 – Asymptomatic	1 562	16.9	478	17.9	485	17.7	184	16.2	415	15.4
1 – Symptomatic but completely ambulatory	5 765	62.4	1 573	59.0	1 737	63.3	755	66.4	1 700	63.0
2 – Symptomatic, up and about more than 50% of waking hours	230	2.5	64	2.4	73	2.7	35	3.1	58	2.1
3 – Symptomatic, confined to bed or chair > 50% of waking hours	106	1.1	25	0.9	30	1.1	14	1.2	37	1.4
4 – Completely disabled; totally confined to bed or chair	38	0.4	9	0.3	17	0.6	6	0.5	6	0.2
Missing	1 544	16.7	516	19.4	403	14.7	143	12.6	482	17.9

	Total (N=9 245)		Oral cavity (N=2 665)		Oropharynx (N=2 745)		Hypopharynx (N=1 137)		Larynx (N=2 698)	
	N	Valid %*	N	Valid %*	N	Valid %*	N	Valid %*	N	Valid %*
Comorbidities										
Peripheral vascular disease	492	5.6	128	5.1	145	5.6	76	6.9	143	5.5
Myocardial infarct	353	4.0	85	3.4	93	3.6	50	4.5	125	4.8
Congestive heart failure	284	3.2	77	3.1	83	3.2	46	4.2	78	3.0
Chronic pulmonary disease	1 710	19.4	443	17.7	451	17.4	253	23.0	563	21.5
Cerebrovascular disease	421	4.8	112	4.5	129	5.0	63	5.7	117	4.5
Dementia	112	1.3	40	1.6	34	1.3	12	1.1	26	1.0
Diabetes without chronic complications	705	8.0	213	8.5	182	7.0	66	6.0	244	9.3
Diabetes with chronic complications	97	1.1	25	1.0	23	0.9	19	1.7	30	1.1
Renal disease	283	3.2	72	2.9	86	3.3	36	3.3	89	3.4
Peptic ulcer disease	359	4.1	112	4.5	122	4.7	48	4.4	77	2.9
Mild liver disease	318	3.6	100	4.0	107	4.1	65	5.9	46	1.8
Moderate to severe liver disease	146	1.7	37	1.5	60	2.3	28	2.5	21	0.8
Paraplegia/hemiplegia	76	0.9	20	0.8	25	1.0	14	1.3	17	0.7
Rheumatologic disease	57	0.6	16	0.6	19	0.7	6	0.5	16	0.6
HIV/Aids	11	0.1	2	0.1	4	0.2	1	0.1	4	0.2
No data available	433		160		152		38		83	
Adapted Charlson Comorbidity Index**										
0	5 359	60.8	1 548	61.8	1 598	61.6	609	55.4	1 604	61.3
1	1 964	22.3	553	22.1	562	21.7	266	24.2	583	22.3
2	783	8.9	224	8.9	207	8.0	127	11.6	225	8.6
3	364	4.1	100	4.0	113	4.4	40	3.6	111	4.2
4	193	2.2	45	1.8	70	2.7	29	2.6	49	1.9
5	93	1.1	18	0.7	28	1.1	16	1.5	31	1.2

	Total (N=9 245)		Oral cavity (N=2 665)		Oropharynx (N=2 745)		Hypopharynx (N=1 137)		Larynx (N=2 698)	
6	34	0.4	9	0.4	9	0.3	8	0.7	8	0.3
7	16	0.2	7	0.3	3	0.1	3	0.3	3	0.1
8	4	0.0	0	0.0	2	0.1	1	0.1	1	0.0
9	1	0.0	1	0.0	0	0.0	0	0.0	0	0.0
10	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
11	1	0.0	0	0.0	1	0.0	0	0.0	0	0.0
No data available	433		160		152		38		83	
Adapted Charlson Comorbidity Index (category)**										
0	5 359	60.8	1 548	61.8	1 598	61.6	609	55.4	1 604	61.3
1-2	2 747	31.2	777	31.0	769	29.7	393	35.8	808	30.9
3-4	557	6.3	145	5.8	183	7.1	69	6.3	160	6.1
>4	149	1.7	35	1.4	43	1.7	28	2.5	43	1.6
No data available	433		160		152		38		83	

* Valid %: percentage not including missing cases in the denominator; ** For more details on the KCE adaptation of the Charlson Comorbidity Index, see section 3.3.5.
HNSCC: Head and neck squamous cell carcinoma; SD: Standard deviation.
Source: BCR – IMA – MZG

Table 79 – Tumour characteristics (HNSCC, incidence 2009-2014)

	Total (N=9 245)		Oral cavity (N=2 665)		Oropharynx (N=2 745)		Hypopharynx (N=1 137)		Larynx (N=2 698)	
	N	%	N	%	N	%	N	%	N	%
Clinical stage										
Reported:	7 444	80.5	1 921	72.1	2 342	85.3	1 012	89.0	2 169	80.4
I*	1 412	19.0	471	24.5	151	6.4	33	3.3	757	34.9
II*	1 068	14.3	344	17.9	251	10.7	69	6.8	404	18.6
III*	1 137	15.3	237	12.3	375	16.0	165	16.3	360	16.6

	Total (N=9 245)		Oral cavity (N=2 665)		Oropharynx (N=2 745)		Hypopharynx (N=1 137)		Larynx (N=2 698)	
IVA*	3 157	42.4	766	39.9	1 268	54.1	559	55.2	564	26.0
IVB*	343	4.6	50	2.6	168	7.2	99	9.8	26	1.2
IVC*	327	4.4	53	2.8	129	5.5	87	8.6	58	2.7
X (missing)	1 801	19.5	744	27.9	403	14.7	125	11.0	529	19.6
Pathological stage**										
Patients who had surgery	*3 518*	*38.1*	*1 957*	*73.4*	*644*	*23.5*	*154*	*13.5*	*763*	*28.3*
Reported:	2 758	78.4	1 619	82.7	462	71.7	124	80.5	553	72.5
I*	905	32.8	568	35.1	128	27.7	9	7.3	200	36.2
II*	433	15.7	306	18.9	75	16.2	7	5.6	45	8.1
III*	398	14.4	209	12.9	82	17.7	18	14.5	89	16.1
IVA*	981	35.6	521	32.2	162	35.1	85	68.5	213	38.5
IVB*	28	1.0	12	0.7	8	1.7	3	2.4	5	0.9
IVC*	13	0.5	3	0.2	7	1.5	2	1.6	1	0.2
X (missing)	760	21.6	338	17.3	182	28.3	30	19.5	210	27.5
Combined stage***										
Reported:	8 250	89.2	2 382	89.4	2 498	91.0	1 041	91.6	2 329	86.3
I*	1 794	21.7	677	28.4	221	8.8	43	4.1	853	36.6
II*	1 119	13.6	392	16.5	264	10.6	74	7.1	389	16.7
III*	1 257	15.2	288	12.1	409	16.4	174	16.7	386	16.6
IVA*	3 408	41.3	919	38.6	1 306	52.3	570	54.8	613	26.3
IVB*	327	4.0	50	2.1	159	6.4	91	8.7	27	1.2
IVC*	345	4.2	56	2.4	139	5.6	89	8.5	61	2.6
X (missing)	995	10.8	283	10.6	247	9.0	96	8.4	369	13.7

* The % for stages I, II, III and IVA, IVB, IVC are computed excluding the X category; ** Limited to patients who had surgery; *** Combined stage combines information from the clinical and pathological stage, where the pathological stage prevails over the clinical stage except when there is clinical proof of distant metastasis; HNSCC: head and neck squamous cell carcinoma.
Source: BCR – IMA

Table 80 – Consistency between clinical and pathological staging - Oral cavity SCC (operated patients, N=1 957)

Clinical stage		p-stage missing	p-stage reported	pI		pII		pIII		pIVA/B		pIVC	
	N	N	N	N	%	N	%	N	%	N	%	N	%
cI	430	60	370 **(100%)**	289	78.1	37	10.0	22	5.9	22	5.9	0	0.0
cII	294	31	263 **(100%)**	59	22.4	126	47.9	45	17.1	33	12.5	0	0.0
cIII	172	21	151 **(100%)**	9	6.0	30	19.9	57	37.7	55	36.4	0	0.0
cIVA/B	470	81	389 **(100%)**	18	4.6	33	8.5	28	7.2	310	79.7	0	0.0
cIVC	12	4	8 **(100%)**	0	0.0	0	0.0	3	37.5	3	37.5	2	25.0
Total known c-stage	1 378	197 (14.3%)	1 181 (85.7%)										
cX	579	141	438 **(100%)**	193	44.1	80	18.3	54	12.3	110	25.1	1	0.2
Total	1 957	338											

Note: Reported percentages are row percentages; absolute numbers and % of cases where clinical and pathological stages are consistent are underlined; SCC: squamous cell carcinoma.
Source: BCR – IMA

Table 81 – Consistency between clinical and pathological staging - Oropharynx SCC (operated patients, N=644)

Clinical stage		p-stage missing	p-stage reported	pI		pII		pIII		pIVA/B		pIVC	
	N	N	N	N	%	N	%	N	%	N	%	N	%
cI	96	25	71 **(100%)**	55	77.5	11	15.5	3	4.2	2	2.8	0	0.0
cII	91	25	66 **(100%)**	11	16.7	39	59.1	6	9.1	10	15.2	0	0.0
cIII	93	18	75 **(100%)**	8	10.7	6	8.0	32	42.7	29	38.7	0	0.0
cIVA/B	184	50	134 **(100%)**	16	11.9	6	4.5	20	14.9	89	66.4	3	2.2
cIVC	13	6	8 **(100%)**	0	0.0	0	0.0	2	28.6	2	28.6	3	42.9
Total known c-stage	477	124 (26%)	353 (74%)										
cX	167	58	109 **(100%)**	38	34.9	13	11.9	19	17.4	38	34.9	1	0.9
Total	644	182											

Note: Reported percentages are row percentages; absolute numbers and % of cases where clinical and pathological stages are consistent are underlined; SCC: squamous cell carcinoma.
Source: BCR – IMA

Table 82 – Consistency between clinical and pathological staging - Hypopharynx SCC (operated patients, N=154)

Clinical stage		p-stage missing	p-stage reported	pI		pII		pIII		pIVA/B		pIVC	
	N	N	N	N	%	N	%	N	%	N	%	N	%
cI	8	3	5 **(100%)**	<u>3</u>	<u>60.0</u>	1	20.0	1	20.0	0	0.0	0	0.0
cII	7	1	6 **(100%)**	1	16.7	<u>3</u>	<u>50.0</u>	2	33.3	0	0.0	0	0.0
cIII	15	5	10 **(100%)**	1	10.0	0	0.0	<u>4</u>	<u>40.0</u>	5	50.0	0	0.0
cIVA/B	99	15	84 **(100%)**	0	0.0	2	2.4	5	6.0	<u>76</u>	<u>90.5</u>	2	2.4
cIVC	2	1	1 **(100%)**	0	0.0	0	0.0	0	0.0	0	0.0	<u>1</u>	<u>100.0</u>
Total known c-stage	131	25 (19.1%)	106 (80.9%)										
cX	23	5	18 **(100%)**	4	22.2	1	5.6	6	33.3	7	38.9	0	0.0
Total	154	30											

Note: Reported percentages are row percentages; absolute numbers and % of cases where clinical and pathological stages are consistent are underlined; SCC: squamous cell carcinoma
Source: BCR – IMA

Table 83 – Consistency between clinical and pathological staging - Larynx SCC (operated patients, N=763)

Clinical stage		Pathological stage											
		p-stage missing	p-stage reported	pI		pII		pIII		pIVA/B		pIVC	
	N	N	N	N	%	N	%	N	%	N	%	N	%
cI	188	53	135 **(100%)**	<u>123</u>	<u>91.1</u>	5	3.7	5	3.7	2	1.5	0	0.0
cII	76	19	57 **(100%)**	21	36.8	<u>22</u>	<u>38.6</u>	6	10.5	8	14.0	0	0.0
cIII	75	9	66 **(100%)**	5	7.6	5	7.6	<u>32</u>	<u>48.5</u>	24	36.4	0	0.0
cIVA/B	200	19	181 **(100%)**	0	0.0	10	5.5	28	15.5	<u>143</u>	<u>79.0</u>	0	0.0
cIVC	3	3	0 **(100%)**	0	0.0	0	0.0	0	0.0	0	0.0	<u>0</u>	<u>0.0</u>
Total known c-stage	542	103 (19%)	439 (81%)										
cX	221	107	114 **(100%)**	51	44.7	3	2.6	18	15.8	41	36.0	1	0.9
Total	763	210											

Note: Reported percentages are row percentages; absolute numbers and % of cases where clinical and pathological stages are consistent are underlined; SCC: squamous cell carcinoma
Source: BCR – IMA

Appendix 6.2. Main diagnostic and staging procedures

Table 84 – Diagnostic and staging procedures performed within three months around the incidence date of HNSCC

Category	Total (N=9 245)		Oral cavity (N=2 665)		Oropharynx (N=2 745)		Hypopharynx (N=1 137)		Larynx (N=2 698)	
	N	%	N	%	N	%	N	%	N	%
Multidisciplinary team meeting (MDT)	7 608	82.3	2 071	77.7	2 358	85.9	1 009	88.7	2 170	80.4
Imaging										
RX thorax	6 772	73.3	2 086	78.3	1 921	70.0	892	78.5	1 873	69.4
RX swallow mechanism/oesophagus	682	7.4	45	1.7	162	5.9	171	15.0	304	11.3
RX larynx	108	1.2	12	0. 5	15	0.6	31	2.7	50	1.9
CT neck	8 548	92.5	2 289	85.9	2 644	96.3	1 111	97.7	2 504	92.8
CT skull	1 700	18.4	494	18.5	554	20.2	272	23.9	380	14.1
MRI neck	2 783	30.1	920	34.5	1 035	37.7	307	27.0	521	19.3
MRI head	589	6.4	274	10.3	188	6.9	48	4.2	79	2.9
PET(/CT)	4 425	47.9	1 093	41.0	1 653	60.2	708	62.3	971	36.0
Ultrasound neck	1 763	19.1	428	16.1	726	26.5	304	26.7	305	11.3
Ultrasound abdomen	3 178	34.4	991	37.2	1 005	36.6	426	37.5	756	28.0
Endoscopy										
Tracheoscopy/Laryngoscopy	7 844	84.9	1 598	60.0	2 478	90.3	1 108	97.5	2 660	98.6
Bronchoscopy	1 874	20.3	465	17.5	582	21.2	312	27.4	515	19.1
Nasal endoscopy	745	8.1	147	5.5	275	10.0	121	10.6	202	7.5
Screening digestive tract	5 445	58.9	1 345	50.5	1 786	65.1	885	77.8	1 429	53.0
Histopathology										
Biopsy of primary tumour	9 127	98.7	2 640	99.1	2 697	98.3	1 110	97.6	2 680	99.3
Lymph node biopsy	320	3.5	68	2.6	156	5.7	46	4.1	50	1.9
Cytology	1 746	18.9	354	13.3	711	25.9	303	26.7	378	14.0

HNSCC: head and neck squamous cell carcinoma; for included RIZIV – INAMI nomenclature codes, we refer to Appendix 3.
Source: BCR – IMA

Appendix 6.3. Main therapeutic procedures

Table 85 – Surgery with curative intent for the primary tumour and lymphadenectomy for HNSCC patients diagnosed in 2009-2014

	Total (N=9 245)		Oral cavity (N=2 665)		Oropharynx (N=2 745)		Hypopharynx (N=1 137)		Larynx (N=2 698)	
	N	%	N	%	N	%	N	%	N	%
Surgery with curative intent	3 518	38.1	1 957	73.4	644	23.5	154	13.5	763	28.3
Surgery with curative intent for the primary tumour + lymphadenectomy	2 313	25.0	1 425	53.5	399	14.5	129	11.4	360	13.3
Surgery with curative intent for the primary tumour only	1 205	13.0	532	20.0	245	8.9	25	2.2	403	14.9
Lymphadenectomy only	356	3.9	54	2.0	166	6.1	79	7.0	57	2.1
Neither surgery with curative intent for the primary tumour nor lymphadenectomy	5 371	58.1	654	24.5	1 935	70.5	904	79.5	1 878	69.6

Table 86 – Main therapeutic procedures (primary treatment) for patients with <u>oral cavity</u> SCC diagnosed in 2009-2014, by clinical stage

	Total (N=2 665)		I (N=471)		II (N=344)		III (N=237)		IVA (N=766)		IVB (N=50)		IVC (N=53)		Unknown (N=744)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Surgery with curative intent	1957	73.4	430	91.3	294	85.5	172	72.6	456	59.5	14	28.0	12	22.6	579	77.8
Surgery only	1024	38.4	365	77.5	142	41.3	44	18.6	99	12.9	6	12.0	3	5.7	365	49.1
Surgery < RT	502	18.8	45	9.6	111	32.3	66	27.9	152	19.8	1	2.0	1	1.9	126	16.9
Surgery < SystRT	340	12.8	15	3.2	34	9.9	53	22.4	161	21.0	7	14.0	4	7.6	66	8.9
Surgery < Syst	43	1.6	4	0.9	3	0.9	1	0.4	16	2.1	0	0.0	3	5.7	16	2.2
Syst < Surgery	12	0.5	1	0.2	3	0.9	3	1.3	4	0.5	0	0.0	0	0.0	1	0.1
Syst < Surgery < RT	18	0.7	0	0.0	0	0.0	1	0.4	13	1.7	0	0.0	1	1.9	3	0.4

	Total (N=2 665)		I (N=471)		II (N=344)		III (N=237)		IVA (N=766)		IVB (N=50)		IVC (N=53)		Unknown (N=744)	
Syst < Surgery < SystRT	12	0.5	0	0.0	0	0.0	4	1.7	8	1.0	0	0.0	0	0.0	0	0.0
Syst < Surgery < Syst	6	0.2	0	0.0	1	0.3	0	0.0	3	0.4	0	0.0	0	0.0	2	0.3
(Syst)RT < Surgery (< adjuvant treatment)	15	0.6	3	0.6	0	0.0	4	1.7	3	0.4	0	0.0	0	0.0	5	0.7
Primary (Syst)RT (no major surgery)	404	15.2	14	3.0	32	9.3	41	17.3	216	28.2	30	60.0	10	18.9	61	8.2
RT only	108	4.1	11	2.3	28	8.1	11	4.6	33	4.3	2	4.0	2	3.8	21	2.8
SystRT	296	11.1	3	0.6	4	1.2	30	12.7	183	23.9	28	56.0	8	15.1	40	5.4
Primary systemic therapy (no major surgery, no RT)	85	3.2	1	0.2	2	0.6	5	2.1	35	4.6	3	6.0	20	37.7	19	2.6
Chemotherapy only	72	2.7	1	0.2	2	0.6	5	2.1	30	3.9	3	6.0	13	24.5	18	2.4
Chemo-/Targeted therapy	13	0.5	0	0.0	0	0.0	0	0.0	5	0.7	0	0.0	7	13.2	1	0.1
Targeted therapy only	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Palliative RT	4	0.2	0	0.0	1	0.3	0	0.0	2	0.3	0	0.0	1	1.9	0	0.0
No cancer treatment	200	7.5	23	4.9	15	4.4	15	6.3	54	7.1	3	6.0	10	18.9	80	10.8

<: followed by; RT: radiotherapy; Syst: systemic therapy (=chemo and/or targeted therapy); (Syst)RT < Surgery (< adjuvant treatment): based on the nomenclature codes impossible to distinguish induction RT followed by surgery from primary RT followed by salvage surgery; adjuvant treatment can be RT and/or systemic treatment after surgery. Source: BCR – IMA

Table 87 – Main therapeutic procedures (primary treatment) for patients with <u>oropharynx</u> SCC diagnosed in 2009-2014, by clinical stage

	Total (N=2 745)		I (N=151)		II (N=251)		III (N=375)		IVA (N=1268)		IVB (N=168)		IVC (N=129)		Unknown (N=403)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Surgery with curative intent	644	23.5	96	63.6	91	36.3	93	24.8	164	12.9	20	11.9	13	10.1	167	41.4
Surgery only	231	8.4	66	43.7	41	16.3	23	6.1	19	1.5	3	1.8	1	0.8	78	19.4
Surgery < RT	169	6.2	25	16.6	40	15.9	30	8.0	37	2.9	1	0.6	2	1.6	34	8.4
Surgery < SystRT	211	7.7	5	3.3	8	3.2	38	10.1	99	7.8	13	7.7	1	0.8	47	11.7
Surgery < Syst	26	0.9	0	0.0	0	0.0	1	0.3	8	0.6	1	0.6	9	7.0	7	1.7
Syst < Surgery	3	0.1	0	0.0	2	0.8	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
Syst < Surgery < RT	1	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
Syst < Surgery < SystRT	3	0.1	0	0.0	0	0.0	1	0.3	1	0.1	1	0.6	0	0.0	0	0.0
Syst < Surgery < Syst	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
(Syst)/RT < Surgery (< adjuvant treatment)	27	1.0	1	0.7	3	1.2	2	0.5	8	0.6	2	1.2	1	0.8	10	2.5
Primary (Syst)RT (no major surgery)	1 724	62.8	45	29.8	152	60.6	249	66.4	971	76.6	115	68.5	42	32.6	150	37.2
RT only	379	13.8	38	25.2	112	44.6	55	14.7	109	8.6	17	10.1	10	7.8	38	9.4
SystRT	1 345	49.0	7	4.6	40	15.9	194	51.7	862	68.0	98	58.3	32	24.8	112	27.8
Primary systemic therapy (no major surgery, no RT)	144	5.2	3	2.0	1	0.4	9	2.4	50	3.9	12	7.1	54	41.9	15	3.7
Chemotherapy only	92	3.4	3	2.0	1	0.4	6	1.6	43	3.4	9	5.4	19	14.7	11	2.7
Chemo-/Targeted therapy	46	1.7	0	0.0	0	0.0	1	0.3	4	0.3	2	1.2	35	27.1	4	1.0
Targeted therapy only	6	0.2	0	0.0	0	0.0	2	0.5	3	0.2	1	0.6	0	0.0	0	0.0
Palliative RT	3	0.1	0	0.0	0	0.0	1	0.3	0	0.0	1	0.6	1	0.8	0	0.0
No treatment	203	7.4	6	4.0	4	1.6	21	5.7	75	6.0	18	10.8	18	14.0	61	15.1

<: followed by; RT: radiotherapy; Syst: systemic therapy (=chemo and/or targeted therapy); (Syst)RT < Surgery (< adjuvant treatment): based on the nomenclature codes impossible to distinguish induction RT followed by surgery from primary RT followed by salvage surgery; adjuvant treatment can be RT and/or systemic treatment after surgery.
Source: BCR – IMA

Table 88 – Main therapeutic procedures (primary treatment) for patients with <u>hypopharynx</u> SCC diagnosed in 2009-2014, by clinical stage

	Total (N=1 137)		I (N=33)		II (N=69)		III (N=165)		IVA (N=559)		IVB (N=99)		IVC (N=87)		Unknown (N=125)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Surgery with curative intent	154	13.5	8	24.2	7	10.1	15	9.1	92	16.5	7	7.1	2	2.3	23	18.4
Surgery only	33	2.9	3	9.1	4	5.8	1	0.6	13	2.3	1	1.0	1	1.2	10	8.0
Surgery < RT	41	3.6	1	3.0	2	2.9	7	4.2	20	3.6	3	3.0	0	0.0	8	6.4
Surgery < SystRT	66	5.8	4	12.1	1	1.5	6	3.6	47	8.4	2	2.0	1	1.2	5	4.0
Surgery < Syst	3	0.3	0	0.0	0	0.0	0	0.0	3	0.5	0	0.0	0	0.0	0	0.0
Syst < Surgery	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Syst < Surgery < RT	6	0.5	0	0.0	0	0.0	1	0.6	5	0.9	0	0.0	0	0.0	0	0.0
Syst < Surgery < SystRT	5	0.4	0	0.0	0	0.0	0	0.0	4	0.7	1	1.0	0	0.0	0	0.0
Syst < Surgery < Syst	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
(Syst)/RT < Surgery (< adjuvant treatment)	6	0.5	0	0.0	0	0.0	1	0.6	3	0.5	2	2.0	0	0.0	0	0.0
Primary (Syst)RT (no major surgery)	795	69.9	22	66.7	57	82.6	136	82.4	404	72.3	68	68.7	31	35.6	77	61.6
RT only	146	12.8	18	54.6	32	46.4	23	13.9	41	7.3	5	5.1	9	10.3	18	14.4
SystRT	649	57.1	4	12.1	25	36.2	113	68.5	363	65.0	63	63.6	22	25.3	59	47.2
Primary systemic therapy (no major surgery, no RT)	94	8.3	0	0.0	1	1.5	6	3.6	31	5.6	12	12.1	38	43.7	6	4.8
Chemotherapy only	54	4.7	0	0.0	1	1.5	4	2.4	23	4.1	10	10.1	12	13.8	4	3.2
Chemo-/Targeted therapy	36	3.2	0	0.0	0	0.0	0	0.0	6	1.1	2	2.0	26	29.9	2	1.6
Targeted therapy only	4	0.4	0	0.0	0	0.0	2	1.2	2	0.4	0	0.0	0	0.0	0	0.0

	Total (N=1 137)		I (N=33)		II (N=69)		III (N=165)		IVA (N=559)		IVB (N=99)		IVC (N=87)		Unknown (N=125)	
Palliative RT	2	0.2	0	0.0	0	0.0	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0
No treatment	86	7.6	3	9.1	4	5.8	7	4.2	27	4.8	10	10.1	16	18.4	19	15.2

<: followed by; RT: radiotherapy; Syst: systemic therapy (=chemo and/or targeted therapy); (Syst)RT < Surgery (< adjuvant treatment): based on the nomenclature codes impossible to distinguish induction RT followed by surgery from primary RT followed by salvage surgery; adjuvant treatment can be RT and/or systemic treatment after surgery. Source: BCR – IMA

Table 89 – Main therapeutic procedures (primary treatment) for patients with larynx SCC diagnosed in 2009-2014, by clinical stage

	Total (N=2 698)		I (N=757)		II (N=404)		III (N=360)		IVA (N=564)		IVB (N=26)		IVC (N=58)		Unknown (N=529)	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Surgery with curative intent	763	28.3	188	24.8	76	18.8	75	20.8	197	34.9	3	11.5	3	5.2	221	41.8
Surgery only	460	17.0	171	22.6	58	14.4	28	7.8	44	7.8	1	3.9	1	1.7	157	29.7
Surgery < RT	192	7.1	15	2.0	13	3.2	30	8.3	94	16.7	0	0.0	0	0.0	40	7.6
Surgery < SystRT	82	3.0	1	0.1	4	1.0	11	3.1	48	8.5	2	7.7	0	0.0	16	3.0
Surgery < Syst	16	0.6	1	0.1	1	0.3	2	0.6	4	0.7	0	0.0	2	3.5	6	1.1
Syst < Surgery	3	0.1	0	0.0	0	0.0	1	0.3	1	0.2	0	0.0	0	0.0	1	0.2
Syst < Surgery < RT	2	0.1	0	0.0	0	0.0	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0
Syst < Surgery < SystRT	6	0.2	0	0.0	0	0.0	2	0.6	4	0.7	0	0.0	0	0.0	0	0.0
Syst < Surgery < Syst	2	0.1	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	1	0.2
(Syst)/RT < Surgery (< adjuvant treatment)	22	0.8	6	0.8	7	1.7	1	0.3	3	0.5	0	0.0	0	0.0	5	1.0
Primary (Syst)RT (no major surgery)	1 673	62.0	528	69.8	302	74.8	260	72.2	310	55.0	18	69.2	30	51.7	225	42.5
RT only	1 082	40.1	510	67.4	265	65.6	101	28.1	48	8.5	1	3.9	8	13.8	149	28.2

		Total (N=2 698)		**I (N=757)**		**II (N=404)**		**III (N=360)**		**IVA (N=564)**		**IVB (N=26)**		**IVC (N=58)**		**Unknown (N=529)**	
	SystRT	591	21.9	18	2.4	37	9.2	159	44.2	262	46.5	17	65.4	22	37.9	76	14.4
Primary systemic therapy (no major surgery, no RT)		58	2.1	0	0.0	1	0.3	7	1.9	23	4.1	2	7.7	13	22.4	12	2.3
	Chemotherapy only	42	1.6	0	0.0	1	0.3	5	1.4	19	3.4	2	7.7	6	10.3	9	1.7
	Chemo-/Targeted therapy	16	0.6	0	0.0	0	0.0	2	0.6	4	0.7	0	0.0	7	12.1	3	0.6
	Targeted therapy only	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Palliative RT		4	0.1	0	0.0	0	0.0	2	0.6	2	0.4	0	0.0	0	0.0	0	0.0
No treatment		178	6.6	35	4.6	18	4.5	15	4.2	29	5.1	3	11.5	12	20.7	66	12.5

<: followed by; RT: radiotherapy; Syst: systemic therapy (=chemo and/or targeted therapy); (Syst)RT < Surgery (< adjuvant treatment): based on the nomenclature codes impossible to distinguish induction RT followed by surgery from primary RT followed by salvage surgery; adjuvant treatment can be RT and/or systemic treatment after surgery.
Source: BCR – IMA

Table 90 – Characteristics of HNSCC patients who received no surgery, no radiotherapy with curative intent and no chemotherapy or targeted treatment (incidence 2009-2014)

	Total (N=680)		Oral cavity (N=204)		Oropharynx (N=206)		Hypopharynx (N=88)		Larynx (N=182)	
	N	%	N	%	N	%	N	%	N	%
Gender										
Male	506	74.4	126	61.8	153	74.3	74	84.1	153	84.1
Female	174	25.6	78	38.2	53	25.7	14	15.9	29	15.9
Age group										
Mean, SD (years)	68.5	SD 13.3	68.6	SD 15.0	66.7	SD 12.3	68.1	SD 11.8	70.4	SD 12.8
Median, range (years)	67	28-102	67	28-98	65	37-102	66.5	46-90	70	33-93
<50 years	34	5.0	14	6.9	9	4.4	3	3.4	8	4.4
50-59 years	171	25.2	54	26.5	61	29.6	23	26.1	33	18.1
60-69 years	167	24.6	47	23.0	53	25.7	24	27.3	43	23.6
70-79 years	138	20.3	30	14.7	47	22.8	17	19.3	44	24.2
80+ years	170	25.0	59	28.9	36	17.5	21	23.9	54	29.7
WHO performance status										
0 – Asymptomatic	54	7.9	14	6.9	18	8.7	8	9.1	14	7.7
1 – Symptomatic but completely ambulatory	305	44.9	92	45.1	94	45.6	39	44.3	80	44.0
2 – Symptomatic, <50% in bed during the day	45	6.6	8	3.9	15	7.3	10	11.4	12	6.6
3 – Symptomatic, >50% in bed, but not bedbound	42	6.2	9	4.4	12	5.8	9	10.2	12	6.6
4 – Bedbound	25	3.7	3	1.5	13	6.3	5	5.7	4	2.2
Missing	209	30.7	78	38.2	54	26.2	17	19.3	60	33.0
Clinical stage										

	Total (N=680)		Oral cavity (N=204)		Oropharynx (N=206)		Hypopharynx (N=88)		Larynx (N=182)	
I	67	9.9	23	11.3	6	2.9	3	3.4	35	19.2
II	42	6.2	16	7.8	4	1.9	4	4.5	18	9.9
III	61	9.0	15	7.4	22	10.7	7	8.0	17	9.3
IVA/B	226	33.2	59	28.9	94	45.6	39	44.3	34	18.7
IVC	58	8.5	11	5.4	19	9.2	16	18.2	12	6.6
X (missing)	226	33.2	80	39.2	61	29.6	19	21.6	66	36.3
Vital status (Follow-up until 14/12/2017)										
Alive	128	18.8	54	26.5	14	6.8	3	3.4	57	31.3
Dead	548	80.6	149	73.0	190	92.2	85	96.6	124	68.1
Lost to follow-up	4	0.6	1	0.5	2	1.0	0	0.0	1	0.6
Survival length in days (Follow-up until 14/12/2017)*										
0 - 90 days	311	46.0	74	36.5	118	57.8	56	63.6	63	34.8
91 – 180 days	76	11.2	23	11.3	24	11.8	10	11.4	19	10.5
181 – 270 days	39	5.8	11	5.4	12	5.9	6	6.8	10	5.5
271 – 360 days	19	2.8	5	2.5	5	2.5	4	4.5	5	2.8
> 360 days	231	34.2	90	44.3	45	22.1	12	13.6	84	46.4
Hospitalisation days within the year before tumour diagnosis	(N=518)		(N=121)		(N=152)		(N=77)		(N=168)	
Mean, SD (days)	20.5	SD 28.2	20.2	SD 24.4	22.3	SD 29.2	24.7	SD 26.9	16.9	SD 30.0
	N	Valid %**	N	Valid %**	N	Valid %**	N	Valid %**	N	Valid %**
Comorbidities										
Peripheral vascular disease	37	7.1	4	3.3	13	8.6	10	13.0	10	6.0
Myocardial infarct	15	2.9	5	4.1	3	2.0	2	2.6	5	3.0

	Total (N=680)		Oral cavity (N=204)		Oropharynx (N=206)		Hypopharynx (N=88)		Larynx (N=182)	
Congestive heart failure	30	5.8	6	5.0	8	5.3	7	9.1	9	5.4
Chronic pulmonary disease	126	24.3	21	17.4	45	29.6	19	24.7	41	24.4
Cerebrovascular disease	53	10.2	10	8.3	18	11.8	11	14.3	14	8.3
Dementia	39	7.5	14	11.6	12	7.9	5	6.5	8	4.8
Diabetes without chronic complications	33	6.4	6	5.0	8	5.3	3	3.9	16	9.5
Diabetes with chronic complications	7	1.4	3	2.5	0	0.0	2	2.6	2	1.2
Renal disease	31	6.0	8	6.6	6	3.9	3	3.9	14	8.3
Peptic ulcer disease	25	4.8	3	2.5	9	5.9	6	7.8	7	4.2
Mild liver disease	27	5.2	7	5.8	9	5.9	7	9.1	4	2.4
Moderate to severe liver disease	15	2.9	2	1.7	9	5.9	4	5.2	0	0.0
Paraplegia/hemiplegia	17	3.3	3	2.5	6	3.9	5	6.5	3	1.8
Rheumatologic disease	4	0.8	1	0.8	2	1.3	0	0.0	1	0.6
HIV/AIDS	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
No data available	*162*		*83*		*54*		*11*		*14*	
Adapted Charlson Comorbidity Index*										
0	261	50.4	70	57.9	62	40.8	30	39.0	99	58.9
1	113	21.8	18	14.9	45	29.6	19	24.7	31	18.5
2	74	14.3	20	16.5	20	13.2	16	20.8	18	10.7
3	27	5.2	4	3.3	12	7.9	5	6.5	6	3.6
4	24	4.6	6	5.0	10	6.6	2	2.6	6	3.6
5	13	2.5	2	1.7	2	1.3	3	3.9	6	3.6
6	2	0.4	0	0.0	0	0.0	1	1.3	1	0.6
7	3	0.6	1	0.8	1	0.7	1	1.3	0	0.0
8	1	0.2	0	0.0	0	0.0	0	0.0	1	0.6

	Total (N=680)		Oral cavity (N=204)		Oropharynx (N=206)		Hypopharynx (N=88)		Larynx (N=182)	
No data available	*162*		*83*		*54*		*11*		*14*	
Adapted Charlson Comorbidity Index (category)***										
0	261	50.4	70	57.9	62	40.8	30	39.0	99	58.9
1-2	187	36.1	38	31.4	65	42.8	35	45.5	49	29.2
3-4	51	9.8	10	8.3	22	14.5	7	9.1	12	7.1
>4	19	3.7	3	2.5	3	2.0	5	6.5	8	4.8
No data available	*162*		*83*		*54*		*11*		*14*	

* Four missing values (lost to follow-up); ** Valid %: percentage not including missing cases in the denominator; *** See section 3.3.5.
Source: BCR – IMA – MZG

Appendix 6.4. Systemic (chemo- and targeted) therapy products for HNSCC patients

Table 91 – Overview of chemo- and targeted therapy products for HNSCC patients (incidence 2009-2014), by combined stage

	Oral cavity				Oropharynx				Hypopharynx				Larynx			
	I-IVB (N= 2326)	IVC (N= 56)	X (N= 283)	Total (N= 2665)	I-IVB (N= 2 359)	IVC (N= 139)	X (N= 247)	Total (N= 2 745)	I-IVB (N= 952)	IVC (N= 89)	X (N= 96)	Total (N= 1 137)	I-IVB (N= 2 268)	IVC (N= 61)	X (N= 369)	Total (N= 2 698)
Chemotherapy	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N	N
L01AA01 (CYCLOPHOSPHAMIDE)	0	0	0	2	1	0	0	1	0	0	1	1	0	0	0	0
L01AA06 (IFOSFAMIDE)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L01BA01 (METHOTREXATE)	13	2	2	17	10	5	2	17	4	5	2	11	17	1	2	20
L01BA03 (RALTITREXED)	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0
L01BA04 (PEMETREXED)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L01BC02 (FLUOROURACIL)	217	29	37	283	374	77	38	489	203	47	17	267	151	22	28	201
L01BC05 (GEMCITABINE)	0	0	0	0	2	0	0	2	2	0	0	2	0	0	0	0
L01BC06 (CAPECITABINE)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L01CA01 (VINBLASTINE)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L01CA02 (VINCRISTINE)	0	0	0	0	1	0	0	1	0	0	1	1	0	0	0	0
L01CA03 (VINDESINE)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L01CA04 (VINORELBINE)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1
L01CB01 (ETOPOSIDE)	2	0	1	3	2	0	0	2	2	0	0	2	0	0	0	0
L01CD01 (PACLITAXEL)	4	2	0	6	13	3	1	17	7	2	1	10	2	0	1	3
L01CD02 (DOCETAXEL)	150	6	30	186	243	19	22	284	143	14	7	164	95	9	19	123
L01DB01 (DOXORUBICIN)	0	0	0	0	2	0	0	2	0	0	1	1	0	0	0	0

	Oral cavity				Oropharynx				Hypopharynx				Larynx			
	I-IVB (N= 2326)	IVC (N= 56)	X (N= 283)	Total (N= 2665)	I-IVB (N= 2 359)	IVC (N= 139)	X (N= 247)	Total (N= 2 745)	I-IVB (N= 952)	IVC (N= 89)	X (N= 96)	Total (N= 1 137)	I-IVB (N= 2 268)	IVC (N= 61)	X (N= 369)	Total (N= 2 698)
L01DB03 (EPIRUBICIN)	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0
L01DC01 (BLEOMYCIN)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L01DC03 (MITOMYCIN)	0	0	0	0	1	0	0	1	1	1	0	2	4	0	4	8
L01XA01 (CISPLATIN)	582	27	59	668	1 220	86	102	1 408	586	54	46	686	519	33	71	623
L01XA02 (CARBOPLATIN)	86	15	15	116	208	26	16	250	88	12	7	107	80	9	12	101
L01XX05 (HYDROXYCARBAMIDE)	2	0	1	3	6	0	0	6	1	0	0	1	1	0	0	1
Targeted therapy																
L01XC06 (CETUXIMAB)	91	11	10	112	265	49	26	340	128	39	13	180	97	13	11	121
L01XE03 (ERLOTINIB)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L01XE10 (EVEROLIMUS)	2	0	0	2	0	0	0	0	1	0	0	1	1	0	0	1

Source: BCR – IMA

Appendix 6.5. Time trends for main diagnostic, staging and therapeutic procedures

Figure 25 – Time trends for diagnostic and staging procedures (HNSCC, incidence 2004-2014)
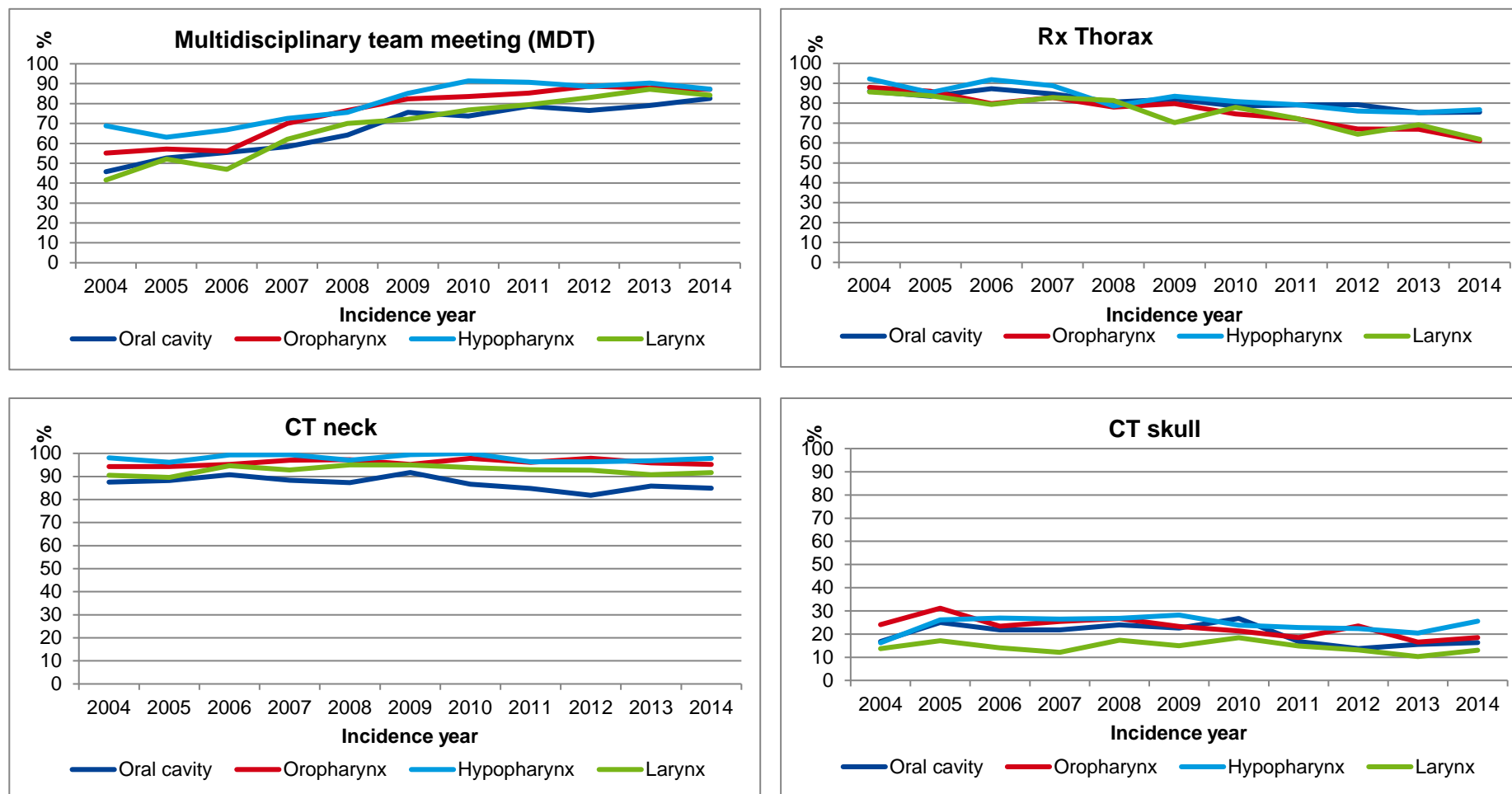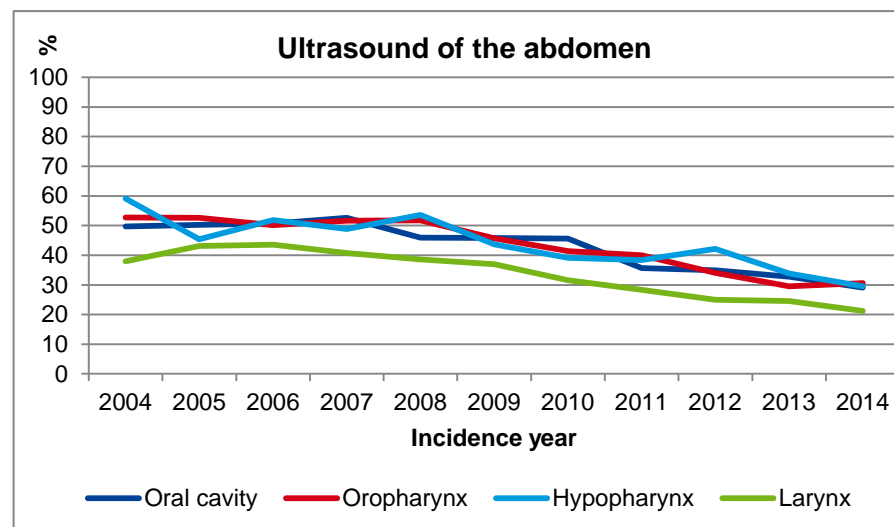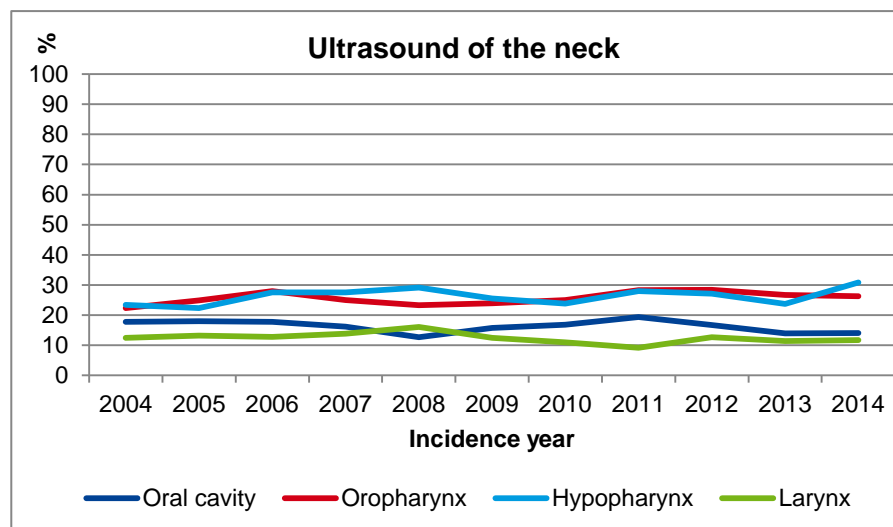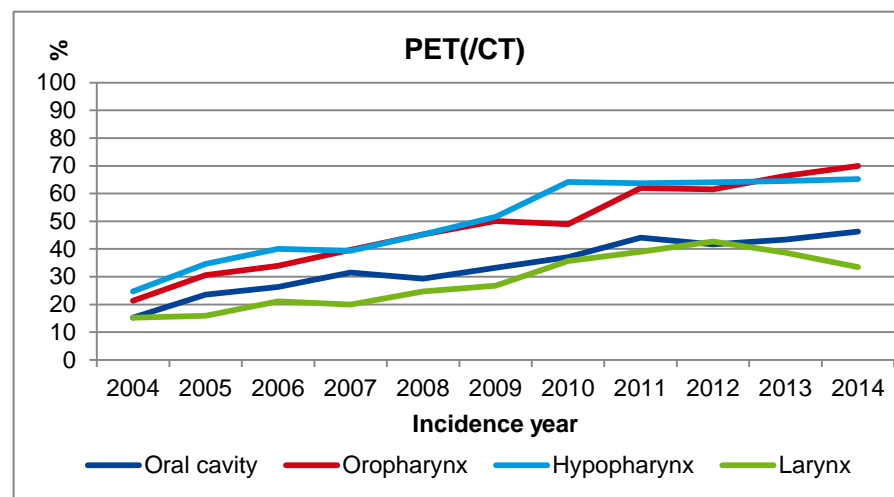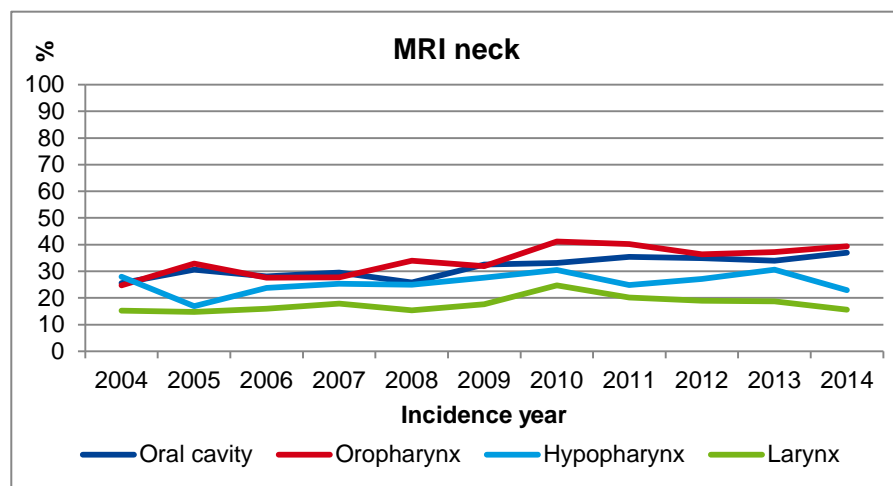
Note: For included RIZIV – INAMI nomenclature codes, we refer to the Appendix 3.
Source: BCR – IMA

Figure 26 – Time trends for main therapeutic procedures for oral cavity (left) and oropharynx (right) SCC (incidence 2004-2014)
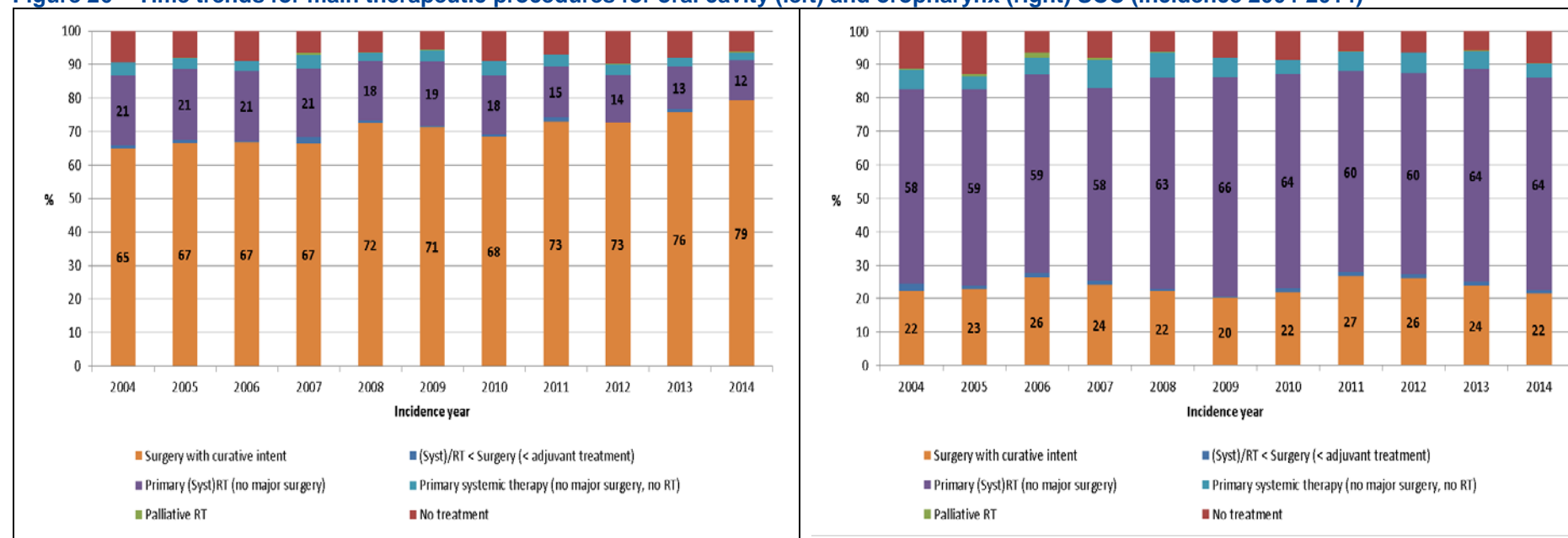
Note: For included RIZIV – INAMI nomenclature codes, we refer to the Appendix 3; the numbers in the bars represent %.
Source: BCR – IMA

Figure 27 – Time trends for main therapeutic procedures for hypopharynx (left) and larynx (right) SCC (incidence 2004-2014)

Note: For included RIZIV – INAMI nomenclature codes, we refer to the Appendix 3; the numbers in the bars represent %.
Source: BCR – IMA

APPENDIX 7.   QUALITY INDICATORS

Appendix 7.1.   Quality of diagnosis and staging in squamous cell carcinoma of the head and neck

Appendix 7.1.1. *Median time between incidence date and start of first treatment with curative intent (DS-1)*

Documentation sheet

Title	Median time between incidence date and start of first treatment with curative intent
Rationale	Timely treatment of (head and neck) cancer is essential, not only to increase the chance for cure and to increase the survival rates, but also to alleviate the symptoms as soon as possible. Indeed, studies on HNSCC patients reported an average tumour doubling time of 96 days[130] to 87 days[131] or even 30 days for the fastest growing tumours.[131] A longer treatment delay for surgery, radiotherapy or chemoradiation is more and more considered as a negative prognostic factor for head and neck cancer patients.[89] The growing number of patients diagnosed with head and neck cancer is imposing a burden on existing diagnostic and treatment resources. The lack of availability of imaging techniques such as PET(/CT) or MRI may delay the discussion at the MDT while the need for complex surgery or intensity-modulated radiotherapy (IMRT) may explain disparities in time delays between centres of treatment.[88] The rarity of HNSCC and the complexity of therapy encourages centralization of care at high-volume centres justifying the transfer of patients from community or regional centres towards academic centres or Head and Neck Oncology centres; however, transition care also contributes to increase time delays before starting the treatment.[89, 132] All these reasons were invoked by the authors of a large cohort study (274 630 HNSCC patients) to explain the sharp increase in the time interval between diagnosis confirmation and start of curative treatment in USA between 1998 and 2011.[132] Patient delays, professional delays or treatment delays to obtain a diagnostic confirmation and to start a treatment with a curative intent may also be long because the symptoms are not specific, they occur in fragile patients and the management requires a multidisciplinary approach with complementary pre-treatment care (dental care, nutritional advise, etc.).[88]
Type of QI	Process
Calculation	Median number of days between the incidence date and the first day of treatment with curative intent Included in analysis: all head and neck SCC patients who received treatment with curative intent within six months of incidence date. Excluded: clinical stage IVC
Target	No target is specified; the data are compared with those from other countries (e.g. Denmark and the Netherlands)
Data sources	• Belgian Cancer Registry (BCR): incidence years 2009 – 2014 • IMA data
Technical definitions	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1) Incidence date as registered at BCR (= date of first microscopic confirmation of malignancy, if not available, date of technical investigation or clinical investigation leading to the diagnosis) Treatment (curative intent) includes: surgery with curative intent (IMA, Table 38 – Table 47), radiotherapy with curative intent (IMA, Table 48), chemotherapy (IMA, Table 54), targeted therapy (IMA, Table 55)
Risk adjustment	None (process indicator)

Title	Median time between incidence date and start of first treatment with curative intent
Limitations	Start date of radiotherapy is not always available in IMA-data; for these cases the start date of radiotherapy is estimated based on the simulation date. If also the simulation date is not available, the start date is estimated based on the end date and duration of the series of similar patients for whom the start date is available in IMA-data.
Subgroup analyses	- Anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx) - Combined stage - Treatment modality - Age at diagnosis - Gender
Sensitivity analyses	None
Benchmarking	Diagnostic centre & centre of main treatment
Comments	Originally, there was the intention to include as well the time period between the multidisciplinary team meeting (MDT) and the start of the first treatment, but since the dates of the MDTs are not sufficiently accurate in the administrative databases used for the project, this part was not elaborated.

Flowchart
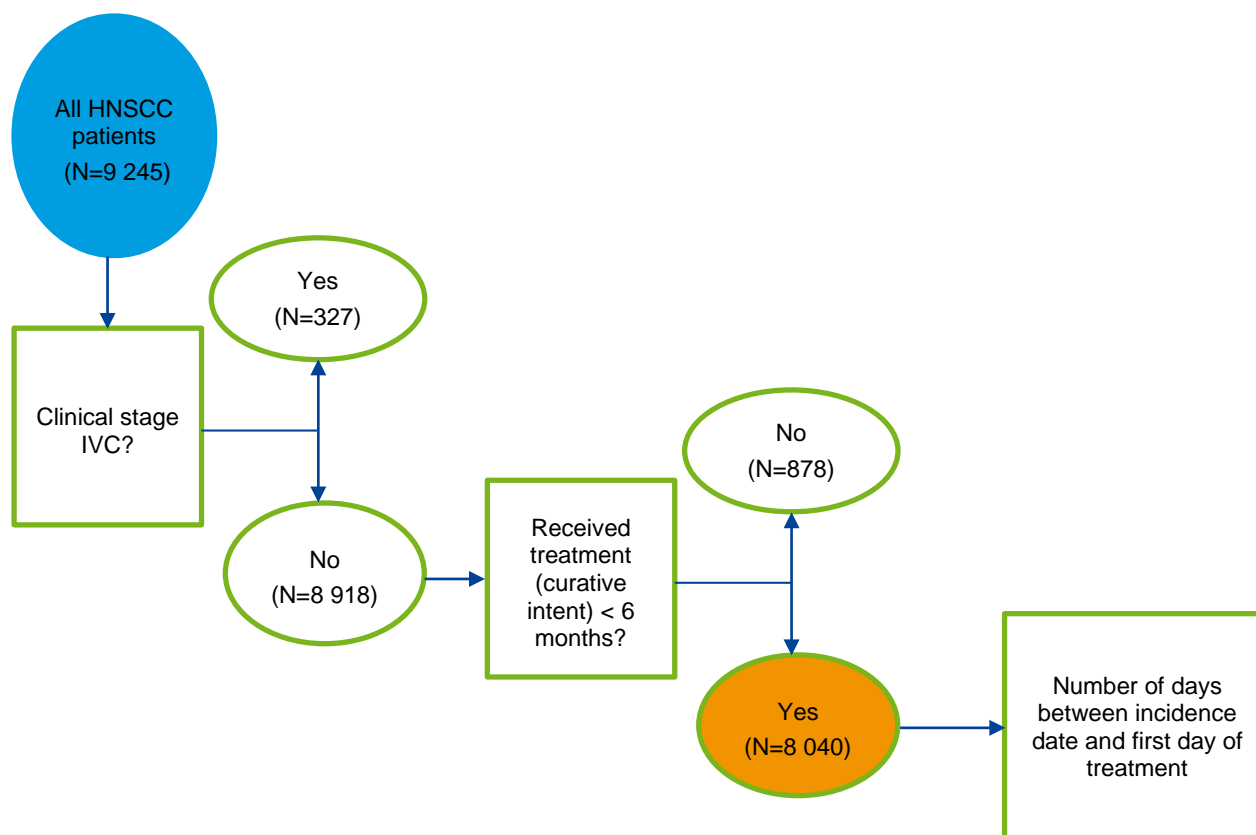
Results

Table 92 – Time (in days) from incidence date to start of first treatment with curative intent by patient, tumour and treatment characteristics (2009-2014)

Characteristics	N	Min$	Q1	Median	Q3	Max
Overall	8 040	0	19	32	46	178
Anatomic site						
Oral cavity	2 354	0	8	27	42	168
Oropharynx	2 339	0	21	34	48	170
Hypopharynx	922	0	24	34	47	169
Larynx	2425	0	21	32	45	178
Gender						
Males	6 082	0	20	32	46	178
Females	1 958	0	16	31	46	170
Age at diagnosis						
<50 years	856	0	17	31	47	176
50-59 years	2 718	0	20	33	47	168
60-69 years	2 661	0	20	32	46	175
70-79 years	1 262	0	18	30	44	173
80+ years	543	0	8	28	43	178
Adapted Charlson Comorbidity Index*						
0	4 837	0	18	31	44	170
1-2	2 826	0	21	34	49	178
3-4	116	0	24	36	51	85
>4	-	-	-	-	-	-
Combined stage						
I	1 711	0	8	28	41	178
II	1 066	0	21	33	47	170
III	1 167	0	22	34	48	132

Characteristics	N	Min$	Q1	Median	Q3	Max
IVA/IVB	3 337	0	21	34	48	176
IVC**	14	0	26	34.5	46	104
X (missing)	745	0	0	26	42	165
Treatment modality						
Surgery with curative intent	3 488	0	1	24	39.5	178
(Syst)/RT < Surgery (< adjuvant treatment)	69	0	0	26	35	69
Primary (Syst)RT (no major surgery)	4 483	0	26	36	49	173
Referred patient*						
No	4 059	0	10	26	39	175
Yes	3 111	0	26	37	52	178
Unknown****	870	0	24	38	53	170

*For 261 patients it was impossible to define the Adapted Charlson Comorbidity Index ; ** Since the analysis is based on combined stage (cTNM and pTNM, see section 4.1.2), combined stage IVC is possible; *** A referred patient is a patient who is treated in a different centre than the centre where the biopsy took place; **** The centre of biopsy is unknown or the centre of first treatment is unknown; $ By definition, the incidence date is the date of the first histopathological confirmation of malignancy. In case this confirmation is not available, the date of the technical procedure or clinical investigation leading to the diagnosis of SCC, was chosen. Note that one case in a group is enough to obtain a min=0.*
Source: BCR – IMA – MZG

Figure 28 – Time from incidence date to first treatment with curative intent, by diagnostic centre (2009-2014)
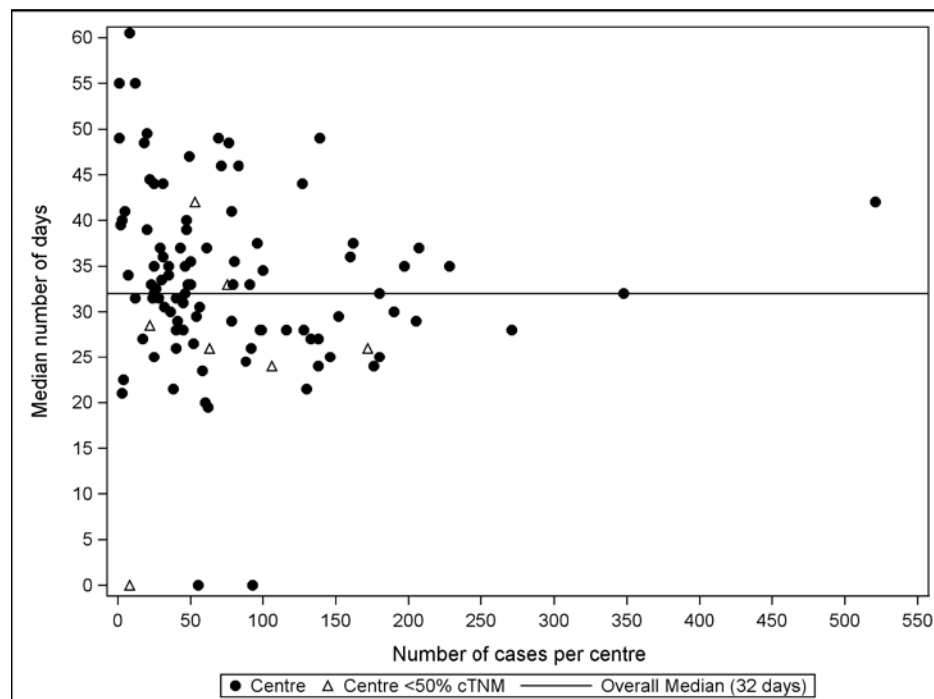
Note: 103 centres reported in the scatter plot; 8 patients were not included in the analyses as they could not be assigned to a diagnostic centre, but their data are included in the analyses for the overall result; centres which reported for less than 50% of their assigned patients' cTNM to the BCR, are represented by an open triangle.
Source: BCR – IMA

International comparison

The French study reported that comorbidities were associated with a longer interval between diagnosis and first treatment for advanced stage HNC, probably due to the need for further explorations and overall care of the patient (e.g. resumption of nutrition, adjustment of treatment) before radiotherapy or chemotherapy.[88]

In the Netherlands where the Dutch Head and Neck Society required in 2001 that 80% of the head and neck cancer patients should be treated within 30 days after diagnosis, only 36% of the patients with an HNSCC were treated within this time frame during a seven year period (2005-2011).[89] Beyond the need for complementary exams and care for advanced disease, patients who were likely to wait significantly longer for treatment had a low socioeconomic status, were treated with radiotherapy or chemoradiation, and were treated in a Head and Neck Oncology Center (HNOC) but diagnosed in a non-HNOC. Despite the longer waiting time when the patient was referred to a HNOC, authors found a better survival for patients who were treated in a HNOC.[89] In searching to improve the quality of care delivered, a Dutch HNOC introduced an integrated care program in 2008, resulting in almost a 20% decrease of waiting time for treatment to a median interval of 29 days.[89]

In the USA, one in four patients experienced treatment delay.[133] A survival analysis on a large cohort of 51 655 patients (2003-2005) demonstrated that patients with time delays of greater than 46 to 52 days had an increased risk of mortality, which was greatest for patients with early-stage disease. The increased risk of death was most consistently detrimental beyond 60 days.[133] Although care transitions to academic facilities are accompanied by an inherent increase in time delay, the improved survival at academic and comprehensive facilities allows to recommend such transfer. However, transitions should be structured to avoid detrimental delays.[133]

In Denmark, decisions were taken by the Danish government and public health services in 2007 to set up a fast track accelerated clinical pathway in order to allow that all new cancer patients be diagnosed and treated without delay. The fast track program focused on multidisciplinary team boards and joint clinics enabling immediate counselling and treatment planning after histopathological diagnosis. The standards foresee 17 calendar days for diagnosis (i.e. time from first healthcare contact with a cancer suspicion until final histopathological diagnosis), 7 days for planning surgery, 11 days for planning radiotherapy, and consequently a total of 24 or 28 calendar days from suspicion of cancer to initiation of surgery or radiotherapy, respectively.

Lyhne et al. (2013) described changes in waiting time at the five Danish HNOC on four-month nationwide cohorts of all consecutive HNSCC patients in 1992 (n=168), 2002 (n=211) and 2010 (n=253), respectively.[86] The median time to diagnosis decreased significantly (from 20 days in 1992 to 13 days in 2010) as did the median interval from diagnosis to treatment start (from 31 days in 1992 to 25 in 2010), leading to a significant decrease of the total pre-treatment time (from 50 days in 1992 to 41 days in 2010). The most pronounced reduction was seen in waiting time for definitive radiotherapy which decreased from 40 to 19 days between 2002 and 2010 (Table 94). Despite this improvement, the median total time from cancer suspicion to start of treatment was still almost six weeks in 2010 and only half of all patients start treatment within the current standards.[86]

Table 93 – Time intervals from diagnosis to first treatment, by treatment modality – Comparison between Belgium and European countries

Treatment modality	Belgium (2009-2014) N=8 040	UK (2013-2014) N=5 932	France (2008 – 2010) N=1 519	The Netherlands (2005 – 2011) N=2 493	Denmark (2010) N=253
	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)	Median (IQR)
Primary surgery	24 (1 – 40)	28 (13 – 43)	27 (12 – 41)	30 (10 – 43)	8 (1 – 28)
Primary RT	36 (26 – 49)	41 (33 – 54)	55 (40 – 71)	42 (31 – 55)	19 (8 – 29)
Overall	32 (19 – 46)	33 (21 – 47)	35 (21 – 54)	37 (24 – 49)	25 (10 – 37)

Table 94 – Time interval between diagnosis (incidence date) and first treatment with curative intent in HNSCC patients - International results

Author	Period covered	Country	Results
Guizard et al., 2016[88]	January 2008 - December 2010	France	Patients registered in cancer registries from four north-western French departments (Calvados, Manche, Somme and Lille) were included (n=1 519). The median time between diagnosis and first treatment was 35 days (Q1: 21 to Q3: 54). The shortest time interval being reported for surgery (median: 27 days, Q1: 12, Q3: 41) and the longest for radiotherapy (median: 54.5 days, Q1: 40, Q3: 71). For 25% of cases, time to the start of radiotherapy was ten weeks or more.
Health and Social Care Information Centre, Tenth Annual Report, 2015[87]	November 2013 - October 2014	England and Wales	During the 1-year audit period, the median interval from diagnosis to first treatment was 33 days. The median interval for surgery was 28 days, for radiotherapy 41 days, while for chemoradiotherapy it was 37 days. For radiotherapy, over a quarter of patients waited beyond 54 days to start treatment. Huge variability in the time to treatment interval was observed both between and within cancer networks.
Murphy et al., 2015[132]	1998-2011	USA	Population based study including 274 630 patients registered in the National Cancer Database. For the entire cohort, the time interval between diagnosis and curative treatment was 19 days in 1998 and rose to 30 days by 2011, for a 58% increase (p<0.0001). When treatment was surgery alone, the median time interval increased from 9 days in 1998 to 24 days in 2011 (167% increase). Relative increases were also observed for definitive RT (from 25 days to 34 days; 36% increase) and CRT (from 28 days to 38 days; 36% increase). The greatest increases in time delays before treatment with curative intent, were observed in patients with advanced-stage disease, treated with CRT, treated at academic facilities, and patients who have a transition in care.

Author	Period covered	Country	Results
Van Harten et al., 2015[89]	2005-2011	The Netherlands	A population based study including 13 140 patients with newly diagnosed head and neck cancer from the Netherlands Cancer Registry reported a median interval between diagnosis and treatment of 37 days (IQR 24–49). Patients who were likely to wait significantly longer for treatment were diagnosed with a tumour in the oropharynx (41 days, IQR 29–54), had advanced stage (IV) disease (40 days, IQR 28–53), had a low socioeconomic status (38 days, IQR 25–50), were treated with radiotherapy or chemoradiation (42 days, IQR 31–55), and were treated in a Head and Neck Oncology Center (HNOC) but diagnosed in a non-HNOC (44 days, IQR 35–55). In this study, only 36% of the patients with an HNSCC were treated within 30 days after diagnosis.
Lyhne et al., 2013[86]	1992, 2002 and 2010	Denmark	Lyhne et al. (2013) described changes in waiting time at the five Danish HNOC on four-month nationwide cohorts of all consecutive HNSCC patients in 1992 (n=168), 2002 (n=211) and 2010 (n=253), respectively. The median interval from diagnosis to treatment start (from 31 days in 1992, to 47 in 2002 and 25 in 2010). The most pronounced reduction was seen in waiting time for definitive radiotherapy which decreased from 40 to 19 days between 2002 and 2010.

Appendix 7.1.2. MRI and/or contrast-enhanced CT of the primary site and draining lymph nodes before treatment (DS-2)

Documentation sheet

Title	Proportion of non-metastatic HNSCC patients who underwent MRI and/or contrast-enhanced CT of the primary site and draining lymph nodes before treatment with curative intent
Rationale	Appropriate imaging helps to improve the accuracy in defining the extent of disease and thus informs the MDT in the treatment planning process.[87] According to the Belgian guidelines, MRI is the preferred technique for primary T- and N-staging in oral cavity SCC and highly recommended in hypopharyngeal, laryngeal and oropharyngeal SCC. However, for all anatomic sites, a contrast-enhanced CT can also replace MRI when (a good) MRI is technically impossible, likely to be distorted, or not timely available.[22, 23]
Type of QI	Process
Calculation	Actual quality indicator: • Numerator: number of patients in whom an MRI and/or CT was obtained before the start of the first treatment • Denominator: all non-metastatic HNSCC patients who received treatment with curative intent Preferred scenario: • Numerator: number of patients in whom an MRI was obtained before the start of the first treatment • Denominator: all non-metastatic HNSCC patients who received treatment with curative intent Alternative scenario:

Title	**Proportion of non-metastatic HNSCC patients who underwent MRI and/or contrast-enhanced CT of the primary site and draining lymph nodes before treatment with curative intent**
	• Numerator: number of HNSCC patients in whom no MRI was performed, who obtained a contrast-enhanced CT before the start of the first treatment • Denominator: all non-metastatic HNSCC patients who received treatment with curative intent
Target	90%
Data sources	• Belgian Cancer Registry (BCR): incidence years 2009 – 2014 • IMA data
Technical definitions	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1) MRI: for oral cavity and oropharyngeal SCC both MRI neck and MRI head nomenclature codes were included while for hypopharyngeal and laryngeal SCC only MRI neck was included; for billing codes (IMA) see Table 26 and Table 27 (Appendix 3.1.2) Contrast-enhanced CT: billing codes (IMA) in Table 24 and Table 25 (Appendix 3.1.2) Treatments: surgery with curative intent (IMA, Table 38 – Table 47), radiotherapy with curative intent (IMA, Table 48), chemotherapy (IMA, Table 54), targeted therapy (IMA, Table 55)
Risk adjustment	None (process indicator)
Limitations	The current nomenclature is not specific enough to isolate 'MRI of the primary tumour'; 'MRI neck' includes MRI of the neck or thorax or abdomen or pelvis. 'MRI head' includes skull, brain, temporal bone, pituitary gland, sinuses, orbital or jaw joints. For CT, this limitation is actually also applicable. Moreover, contrast-enhanced CT cannot be distinguished from CT.
Subgroup analyses	- Anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx) - Clinical stage - Treatment modality - Age at diagnosis - Gender
Sensitivity analyses	PET(/CT) versus no PET(/CT) in HNSCC patients who received treatment with curative intent and for whom neither an MRI nor a CT was recorded (IMA, Table 28)
Benchmarking	Main treatment centre

Availability of imaging equipment in Belgium

For the period under study (2009-2014), there was no official registry of the imaging equipment available in Belgium, yet programming rules were installed to limit the number of heavy medical imaging equipment.

For example, the number of accredited **PET scans were limited to thirteen** for the whole country by the law of 27 April 2005.[134] The steady grow in expenses linked to PET scans exams year after year let us however suppose that more PET scans were actually in activity.[135] At the end of 2008, **92 MRI units were accredited** in Belgium (+ four non-accredited MRI).[136] For this period, no programing rules were set up for CT scans and their total number was unknown. However, in 2007, CT scan exams represented 3.5 times the number of MRI exams for all medical indications together (1 778 481 CT exams versus 509 759 MRI exams).[136]

Since 3 February 2016, the registration of heavy medical imaging equipment is mandatory.[137] On 1 January 2018, the following equipment was **accredited** in Belgium for medical purposes (Source: FPS Public Health; accessed on https://www.health.belgium.be/en/node/24107, 9 March 2018):

- 262 CT

- 1 PET and 29 PET(/CT)

- 134 SPECT-CT

- 121 MRI (without taking into account MRI for research purposes)

Flowchart
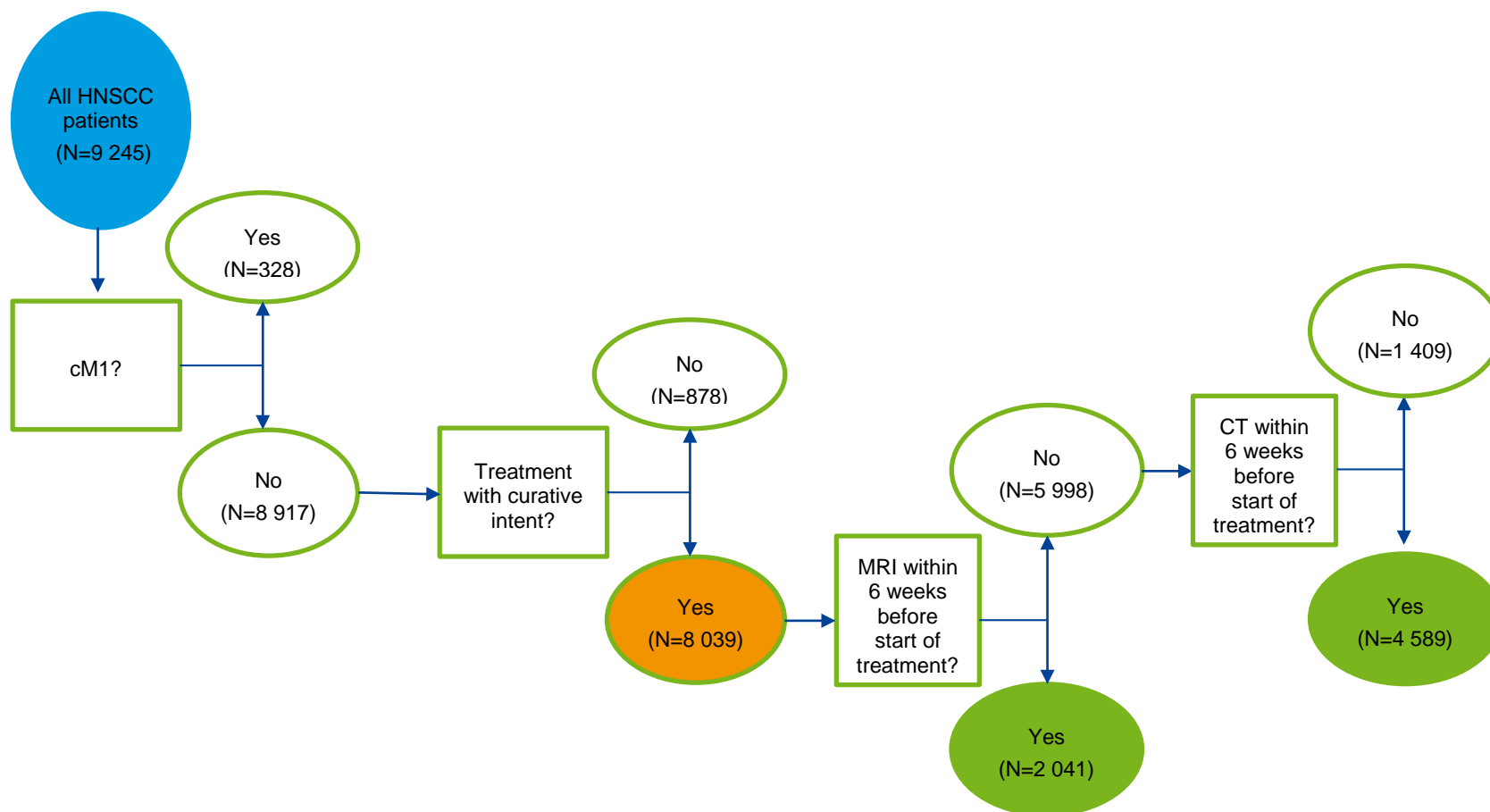
Results

Table 95 – Proportion of HNSCC patients who received treatment with curative intent in whom an MRI and/or CT was obtained within six weeks before the start of the first treatment, by patient and tumour characteristics (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	8 039	6 630	82.5
Anatomic site			
Oral cavity	2 354	1 762	74.9
Oropharynx	2 339	2 089	89.3
Hypopharynx	922	825	89.5
Larynx	2 424	1 954	80.6
Gender			
Males	6 081	5 094	83.8
Females	1 958	1 536	78.4
Age at diagnosis			
<50 years	856	699	81.7
50-59 years	2 717	2 293	84.4
60-69 years	2 661	2 221	83.5
70-79 years	1 262	1 022	81.0
80+ years	543	395	72.7
Clinical stage			
I	1 341	991	73.9
II	1 021	854	83.6
III	1 049	940	89.6
IVA/B	3 106	2 772	89.2
X (missing)	1 522	1 073	70.5
Treatment modality			
Surgery with curative intent	3 488	2 460	70.5
(Syst)RT < Surgery (< adjuvant treatment*)	69	45	65.2
Primary (Syst)RT (no major surgery)	4 482	4 125	92.0

*Note: * Adjuvant treatment can be either systemic treatment or radiotherapy.*
Source: BCR – IMA

Table 96 – Proportion of HNSCC patients who received treatment with curative intent in whom an MRI and/or CT was obtained within six weeks before the start of the first treatment, by anatomic site and clinical stage (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Oral cavity	2 354	1 762	74.9
I	447	296	66.2
II	326	258	79.1
III	217	187	86.2
IVA/B	719	597	83.0
X (missing)	645	424	65.7
Oropharynx	2 339	2 089	89.3
I	142	109	76.8
II	246	208	84.6
III	344	318	92.4
IVA/B	1 280	1 194	93.3
X (missing)	327	260	79.5
Hypopharynx	922	825	89.5
I	30	26	86.7
II	64	52	81.3
III	152	146	96.1
IVA/B	576	519	90.1
X (missing)	100	82	82.0
Larynx	2 424	1 954	80.6
I	722	560	77.6
II	385	336	87.3
III	336	289	86.0
IVA/B	531	462	87.0
X (missing)	450	307	68.2

Source: BCR – IMA

Table 97 – Proportion of HNSCC patients who received treatment with curative intent in whom either an MRI or a CT was obtained within six weeks before the start of the first treatment, by patient and tumour characteristics

	HNSCC patients who received treatment with curative intent	MRI within six weeks before the start of the first treatment		CT within six weeks before the start of the first treatment without MRI within six weeks	
	Denominator	Numerator	Proportion (%)	Numerator	Proportion (%)
Overall	8 039	2 041	25.4	4 589	57.1
Anatomic site					
Oral cavity	2 354	737	31.3	1 025	43.5
Oropharynx	2 339	738	31.6	1 351	57.8
Hypopharynx	922	196	21.3	629	68.2
Larynx	2 424	370	15.3	1 584	65.3
Gender					
Males	6 081	1 508	24.8	3 586	59.0
Females	1 958	533	27.2	1 003	51.2
Age at diagnosis					
<50 years	856	260	30.4	439	51.3
50-59 years	2 717	716	26.4	1 577	58.0
60-69 years	2 661	683	25.7	1 538	57.8
70-79 years	1 262	296	23.5	726	57.5
80+ years	543	86	15.8	309	56.9
Clinical stage					
I	1 341	236	17.6	755	56.3
II	1 021	265	26.0	589	57.7
III	1 049	298	28.4	642	61.2
IVA/B	3 106	954	30.7	1 818	58.5
X (missing)	1 522	288	18.9	785	51.6
Treatment modality					

	HNSCC patients who received treatment with curative intent	MRI within six weeks before the start of the first treatment		CT within six weeks before the start of the first treatment without MRI within six weeks	
	Denominator	Numerator	Proportion (%)	Numerator	Proportion (%)
Surgery with curative intent	3 488	863	24.7	1 597	45.8
(Syst)/RT < Surgery (< adjuvant treatment)	69	9	13.0	36	52.2
Primary (Syst)RT (no major surgery)	4 482	1 169	26.1	2 956	66.0

Source: BCR – IMA

Table 98 – Proportion of HNSCC patients who received treatment with curative intent without pre-treatment MRI or a CT, in whom a PET(/CT) was performed within six weeks before the start of first treatment (2009-2014)

	Number of patients	%
HNSCC patients who received treatment with curative intent in whom no MRI or CT was obtained within six weeks before the start of the first treatment	1 409	100.0
PET(/CT) within six weeks before start of the first treatment	143	10.1
No PET(/CT) within six weeks before start of the first treatment	1 266	89.9

Source: BCR – IMA

Table 99 – Proportion of HNSCC patients who received treatment with curative intent in whom neither an MRI nor a CT was performed within six weeks before the start of first treatment (N=1 409), by anatomic site and clinical stage (2009-2014)

Characteristics	Number of patients	%
Oral cavity	**592**	**100.0**
I	151	25.5
II	68	11.5
III	30	5.1
IVA/B	122	20.6

Characteristics	Number of patients	%
X (missing)	221	37.3
Oropharynx	**250**	**100.0**
I	33	13.2
II	38	15.2
III	26	10.4
IVA/B	86	34.4
X (missing)	67	26.8
Hypopharynx	**97**	**100.0**
I	4	4.1
II	12	12.4
III	6	6.2
IVA/B	57	58.8
X (missing)	18	18.6
Larynx	**470**	**100.0**
I	162	34.5
II	49	10.4
III	47	10.0
IVA/B	69	14.7
X (missing)	143	30.4

Source: BCR – IMA

International comparison

Table 100 – MRI and/or CT of the primary site and draining lymph nodes before treatment in HNSCC patients - International results

Author	Period covered	Country	Results
Eskander et al., 2016[90]	1993–2010	Ontario	5 720 patients were diagnosed with a HNSCC (oral cavity, oropharynx, hypopharynx, and/or larynx). In 2010, preoperative head and neck (incl. **CT, MRI and neck US**) and chest imaging was performed in **71.8%** (4 105 of 5 720) and 82.5% (4 719 of 5 720) of patients, respectively. Statistically significant differences were observed between largest volume surgeons and lowest volume surgeons (85.2% vs. 57.6% of their patients underwent preoperative head and neck imaging; p<0.001) as well as between largest volume hospitals and lowest volume hospitals (83.1% vs. 57.2%; p<0.001).
Information Services division Scotland, 2016[138]	April 2014 - March 2015	Scotland	Of the 1 149 patients diagnosed in Scotland with head and neck cancer in the one year study period, 96% (1 100) had a definitive diagnosis recorded prior to treatment. **90%** of patients diagnosed with an HNSCC received **radiological staging with CT and/or MRI** prior to treatment (1 035/1 149), falling short of the 95% target adopted in this country. There was considerable variation in performance both between and within regional networks, ranging from 73% to 100% of patients, which was (partly) explained by the inclusion of patients who refused treatment or died before treatment.
Health and Social Care Information Centre, Tenth Annual Report, 2015[87]	November 2013 - October 2014	England and Wales	During the 1-year audit period, a total of 7 252 patients were diagnosed with a HNSCC, discussed at a MDT and received treatment (including palliative intent). Among them, 5 963 (**82.2%**) had a **PET(/CT) , CT, MRI or ultrasound** prior to treatment (10.3% had a PET(/CT), 68.2% had a CT, 49.6% a MRI, 22.4% a US). Five networks on 15 reported 90% of head and neck imaging before starting treatment whereas in one network, only 55.3% of patients had imaging before treatment.

Appendix 7.1.3. T, N and M staging in new cases of SCC of the head and neck (DS-3)

Documentation sheet

Title	a) **Proportion of patients with HNSCC who have their cTNM stage reported to the Belgian Cancer Registry (BCR)**
	b) **Proportion of patients with HNSCC who had surgery, who have their pTNM stage reported to the BCR**
Rationale	Staging is an essential step in the clinical cancer pathway, as it helps in planning the treatment (or the renouncement of treatment) and in predicting the patient's prognosis.
	In Belgium, cancer stage reporting is one of the legal obligations of the responsible physician of the MDT in order to keep the accreditation as oncological care program. Despite this legal requirement, the reporting of the clinical stage to the BCR is not yet optimal and there is also a high variability between centres.[85]
	The other source of information for the staging process are the pathology laboratories. They encode the received specimens following classification rules approved by the Consilium Pathological Belgicum. In Flanders most of the laboratories follow the Codap-2007 classification. Various coding systems are used in the Walloon and Brussels Capital Regions. Every (pre) malignant diagnosis is encoded and transferred to the BCR, accompanied by the protocols as stated in the law.[85]
	These data (clinical and pathological) are then linked by tumour, and quality control and consistency checks are performed. In more complex cases, the data source is consulted to provide additional information.[85]
	As staging clearly contributes to a high quality cancer care, it was selected as quality indicator. However, in reality it is impossible to check the medical files of all HNSCC patients in Belgium, and therefore a proxy approach was used by evaluating the quality of the data transferred to the BCR.
Type of QI	Process
Calculation	a) Numerator: number of patients who have their cTNM reported to the BCR
	Denominator: all patients diagnosed with HNSCC
	b) Numerator: number of patients who have their pTNM reported to the BCR
	Denominator: number of HNSCC patients treated with surgery with curative intent
Target	95%
Data sources	• Belgian Cancer Registry (BCR): incidence years 2009 – 2014
	• IMA data (for b)
Technical definitions	a) Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1)
	b) Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1)
	Treatment: surgery with curative intent (IMA, Table 38 – Table 47)
Risk adjustment	None (process indicator)
Limitations	It was not possible to distinguish cases not reported to BCR from those reported as unknown.
Subgroup analyses	- Anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx)
	- Treatment modality (only for cTNM)
	- Age at diagnosis

Title	a) **Proportion of patients with HNSCC who have their cTNM stage reported to the Belgian Cancer Registry (BCR)**
	b) **Proportion of patients with HNSCC who had surgery, who have their pTNM stage reported to the BCR**
	- Gender
Sensitivity analyses	Patients with HNSCC who were vs. were not discussed during a multidisciplinary team meeting (MDT)
Benchmarking	a) Centre of first treatment
	b) Centre of main treatment

Flowchart

A) Proportion of patients with HNSCC who have their cTNM stage reported to the Belgian Cancer Registry (BCR)
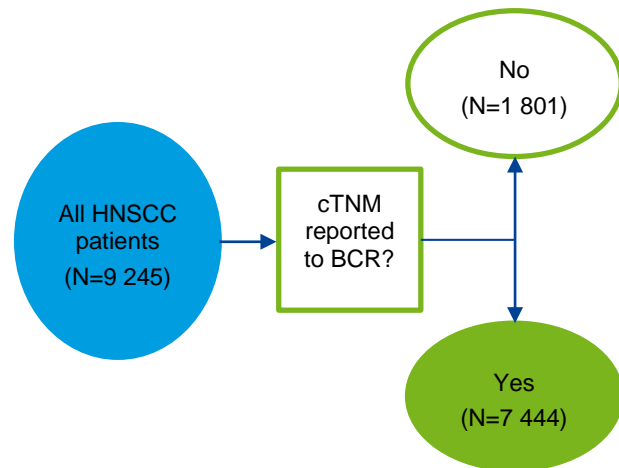
B) Proportion of patients with HNSCC who had surgery, who have their pTNM stage reported to the BCR
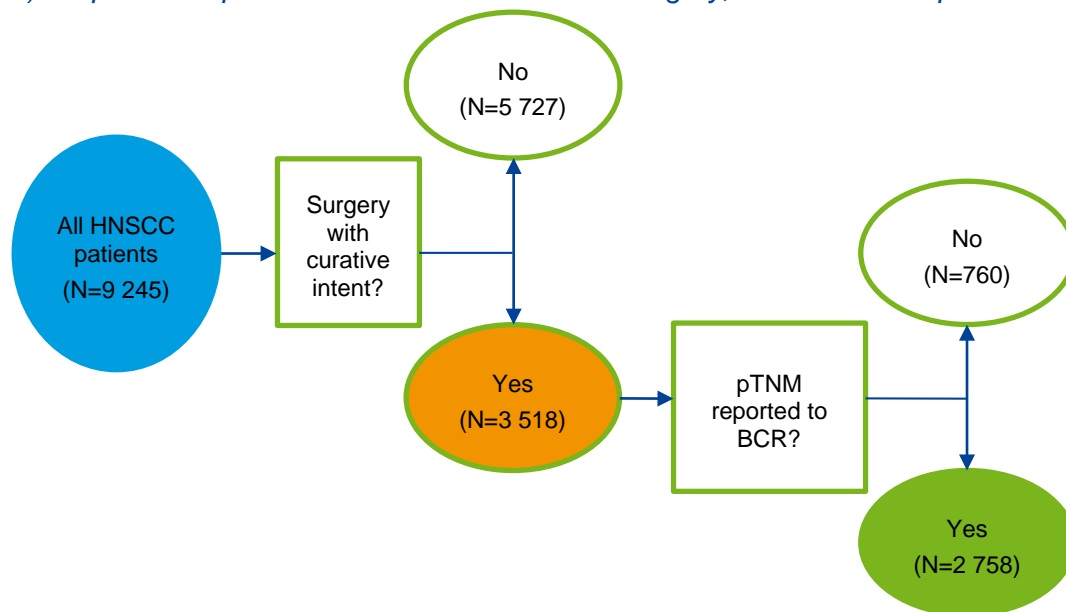
Results

Table 101 – Proportion of patients with HNSCC who have their cTNM stage reported to the BCR, by patient and tumour characteristics (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	9 245	7 444	80.5
Anatomic site			
Oral cavity	2 665	1 921	72.1
Oropharynx	2 745	2 342	85.3
Hypopharynx	1 137	1 012	89.0
Larynx	2 698	2 169	80.4
Gender			
Males	7 017	5 724	81.6
Females	2 228	1 720	77.2
Age at diagnosis			
<50 years	930	739	79.5
50-59 years	3 058	2 513	82.2
60-69 years	3 047	2 499	82.0
70-79 years	1 481	1 159	78.3
80+ years	729	534	73.3
Treatment modality			
Surgery with curative intent	3 518	2 528	71.9
(Syst)/RT < Surgery (< adjuvant treatment*)	70	50	71.4
Primary (Syst)RT (no major surgery)	4 596	4 083	88.8
Primary systemic therapy (no major surgery, no RT)	381	329	86.4
Palliative RT	13	13	100.0
No treatment	667	441	66.1

* Adjuvant treatment: systemic treatment and/or radiotherapy.
Source: BCR – IMA

Table 102 – Proportion of patients with HNSCC who have their cTNM stage reported to the BCR, by anatomic site and by discussion on multidisciplinary team meeting (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Total			
No MDT	1 637	802	49.0
MDT	7 608	6 642	87.3
Oral cavity	2 665	1 921	72.1
No MDT	594	250	42.1
MDT	2 071	1 671	80.7
Oropharynx	2 745	2 342	85.3
No MDT	387	219	56.6
MDT	2 358	2 123	90.0
Hypopharynx	1 137	1 012	89.0
No MDT	128	72	56.3
MDT	1 009	940	93.2
Larynx	2 698	2 169	80.4
No MDT	528	261	49.4
MDT	2 170	1 908	87.9

Source: BCR – IMA

Table 103 – Proportion of patients with HNSCC who had surgery with curative intent, who have their pTNM stage reported to the BCR, by patient and tumour characteristics (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	3 518	2 758	78.4
Anatomic site			
Oral cavity	1 957	1 619	82.7
Oropharynx	644	462	71.7
Hypopharynx	154	124	80.5
Larynx	763	553	72.5
Gender			
Males	2 487	1 948	78.3
Females	1 031	810	78.6
Age at diagnosis			
<50 years	440	344	78.2
50-59 years	1 189	943	79.3
60-69 years	1 088	868	79.8
70-79 years	543	413	76.1
80+ years	258	190	73.6

Source: BCR – IMA

Table 104 – Proportion of patients with HNSCC who had surgery with curative intent, who had their pTNM stage reported to the BCR, by pathological stage (2009-2014)

	N=2 758	Proportion (%)
Pathological stage		
I	905	32.8
II	433	15.7
III	398	14.4
IVA/B	1 009	36.6
IVC	13	0.5

Note: For 760 cases pTNM was missing (i.e. either reported as X or not reported at all).
Source: BCR – IMA

Table 105 – Proportion of patients with HNSCC who had surgery with curative intent, who have their pTNM stage reported to the BCR, by anatomic site and by discussion on multidisciplinary team meeting (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Total			
No MDT	679	438	64.5
MDT	2 839	2 320	81.7
Oral cavity	1 957	1 619	82.7
No MDT	418	309	73.9
MDT	1 539	1 310	85.1
Oropharynx	644	462	71.7
No MDT	97	50	51.5
MDT	547	412	75.3
Hypopharynx	154	124	80.5
No MDT	9	7	77.8
MDT	145	117	80.7
Larynx	763	553	72.5
No MDT	155	72	46.5
MDT	608	481	79.1

Source: BCR – IMA

International comparison

Table 106 – T, N and M staging in new cases of HNSCC - International results

Author	Period covered	Country	Results
Health and Social Care Information Centre, Tenth Annual Report, 2015[87]	November 2013 - October 2014	England and Wales	During the study period, 86.8% (7 175/8 267) of HNSCC patients had their **pre-treatment staging recorded**; among the fifteen cancer networks, nine attained more than 85%, whereas four reached less than 80%. The highest returns were observed in South Wales (99.3%) and the lowest in Thames Valley with 76.2% of staging recorded. The proportion of patients with unknown pre-treatment staging was 16.3% for oral cavity, 13.9% for oropharynx, 11.6% for hypopharynx, and 11.4% for larynx SCC.
			Among patients who had surgery, 81.6% (2 864/3 510) had their **post-surgical histopathological staging** recorded. While six cancer networks attained more than 85%, the gap between highest and lowest performing cancer networks has significantly decreased compared to the previous year.
Ramos et al., 2015[139]	2006 – 2008	Spanish island of Mallorca (around 800 000 inhabitants)	In total 359 head and neck cancers were reported to the Mallorca Cancer Registry; the completeness of registration was very low (T: 42.3% (95% CI: 37.3 - 47.5), N: 41.2% (95% CI: 36.2 - 46.4), M: 32.9% (95% CI: 28.2 - 37.9) and stage: 25.1% (95% CI: 20.9 - 29.8)).

Appendix 7.1.4. FDG-PET(/CT) before treatment (DS-4)

Documentation sheet

Title	Proportion of patients with HNSCC who underwent FDG-PET(/CT) before start of treatment

Rationale	Recommendations in the KCE guidelines (KCE reports 227 & 256):
	
	 Perform a whole-body FDG-PET(/CT) for the evaluation of metastatic spread and/or the detection of second primary tumours:
	    o in patients with stage III and IV oral cavity cancer, and
	    o in oral cavity cancer patients with high-risk features irrespective of the locoregional staging (e.g. heavy smokers).
	
	 In patients with stage I and II oropharyngeal, hypopharyngeal and laryngeal cancer and with low-risk features (e.g. no smoking), a whole-body FDG-PET(/CT) is not routinely recommended for the evaluation of metastatic spread and/or the detection of second primary tumours.
	
	 After discussion with the experts it was decided to expand both parts of the analyses (i.e. stages I-II and stages III-IV) to all HNSCC (i.e. all anatomic sites).

Type of QI	Process
Calculation	• **Numerator**: number of patients in whom a whole-body FDG-PET(/CT) was obtained before the start of the first treatment **Denominator**: number of patients with clinical stage I and II HNSCC who received any treatment • **Numerator**: number of patients in whom a whole-body FDG-PET(/CT) was obtained before the start of the first treatment **Denominator**: number of patients with clinical stage III and IV HNSCC who received non-palliative treatment
Target	• Stage I-II: ≤ 5% • Stage III-IV: ≥ 90%
Data sources	• Belgian Cancer Registry (BCR): incidence years 2009 – 2014 • IMA data
Technical definitions	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1) FDG-PET(/CT) : billing codes (IMA) in Table 28 (Appendix 3.1.2) Treatments: surgery with curative intent (IMA, Table 38 – Table 47), radiotherapy with curative intent (IMA, Table 48), chemotherapy (IMA, Table 54), targeted therapy (IMA, Table 55), palliative radiotherapy (Table 49)
Risk adjustment	None (process indicator)
Limitations	No reliable information available about risk factors in the used databases (e.g. smoking, alcohol consumption)
Subgroup analyses	- Anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx) - Clinical stage - Treatment modality - Age at diagnosis - Gender
Sensitivity analyses	/
Benchmarking	Main treatment centre

Flowchart HNSCC stage I-II

Flowchart HNSCC stage III-IV
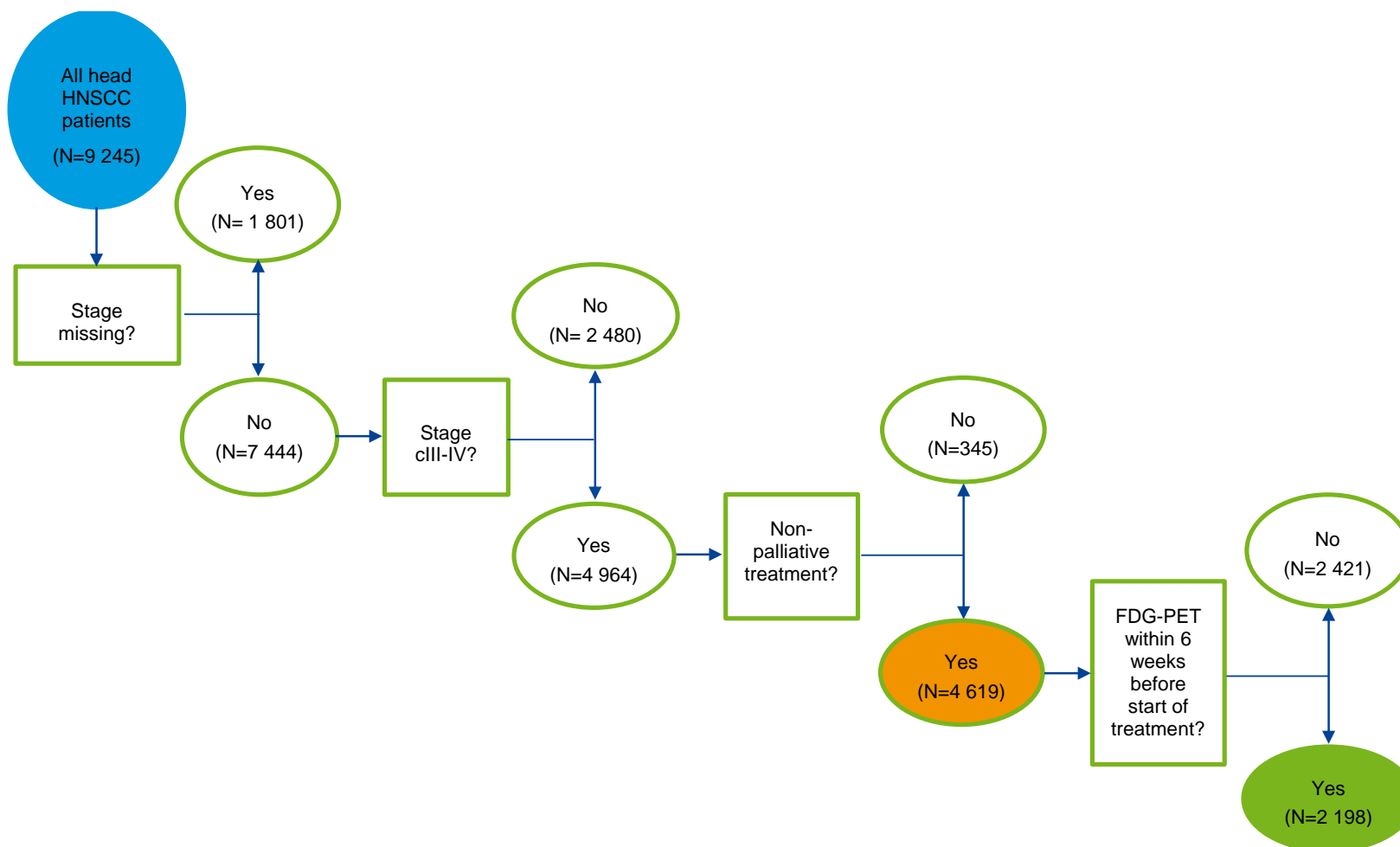
Results

Table 107 – Proportion of clinical stage I-II HNSCC patients who underwent any treatment in whom a whole-body FDG-PET(/CT) was obtained within six weeks before start of the first treatment, by patient, tumour, and treatment characteristics (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	2 372	544	22.9
Anatomic site			
Oral cavity	777	174	22.4
Oropharynx	392	141	36.0
Hypopharynx	95	36	37.9
Larynx	1 108	193	17.4
Gender			
Males	1 782	388	21.8
Females	590	156	26.4
Age at diagnosis			
<50 years	251	63	25.1
50-59 years	734	177	24.1
60-69 years	760	186	24.5
70-79 years	426	86	20.2
80+ years	201	32	15.9
Clinical stage			
I	1 345	220	16.4
II	1 027	324	31.5
Treatment modality			
Surgery with curative intent	1 190	253	21.3
(Syst)/RT < Surgery (< adjuvant treatment*)	20	6	30.0
Primary (Syst)RT (no major surgery)	1 152	283	24.6
Primary systemic therapy (no major surgery, no RT)	9	2	22.2
Palliative RT	1	0	0.0

Adjuvant treatment: systemic treatment and/or radiotherapy.
Source: BCR – IMA

Table 108 – Proportion of clinical stage III-IV HNSCC patients who underwent non-palliative treatment in whom a whole-body FDG-PET(/CT) was obtained within six weeks before start of the first treatment, by patient, tumour, and treatment characteristics (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	4 619	2 198	47.6
Anatomic site			
Oral cavity	1 021	393	38.5
Oropharynx	1 805	960	53.2
Hypopharynx	848	455	53.7
Larynx	945	390	41.3
Gender			
Males	3 596	1 716	47.7
Females	1 023	482	47.1
Age at diagnosis			
<50 years	466	231	49.6
50-59 years	1 664	793	47.7
60-69 years	1 634	820	50.2
70-79 years	637	289	45.4
80+ years	218	65	29.8
Clinical stage			
III	1 076	439	40.8
IVA/B	3 274	1 608	49.1
IVC	269	151	56.1
Treatment modality			
Surgery with curative intent	1 338	525	39.2
(Syst)/RT < Surgery (< adjuvant treatment*)	30	9	30.0
Primary (Syst)RT (no major surgery)	2 931	1 491	50.9
Primary systemic therapy (no major surgery, no RT)	320	173	54.1

* Adjuvant treatment: systemic treatment and/or radiotherapy.
Source: BCR – IMA

International comparison

Table 109 – FDG-PET(/CT) before treatment - International results

Author	Period covered	Country	Results
Health and Social Care Information Centre, Tenth Annual Report, 2014[87]	November 2013 - October 2014	England and Wales	During the study period, 10.6% (721/6 798) of patients were recorded as having undergone PET(/CT) prior to treatment; 23.0% for nasopharynx, 19.3% for oropharynx, 15.5% for hypopharynx, 10.3% for major salivary glands, 8.8% for bone tumours (mandible and maxilla), 7.6% for nasal cavity and sinus, 4.8% for larynx, and 4.6% for oral cavity SCC.

Appendix 7.2. Quality of treatment in squamous cell carcinoma of the head and neck

Appendix 7.2.1. Single modality treatment stage I-II (T-1)

Documentation sheet

Title	Proportion of patients with early stage (cI or cII) HNSCC who were treated with a single-modality approach
Rationale	In patients with early stage (cI or cII) squamous cell carcinoma of the head and neck (HNSCC), a single-modality treatment is preferred in order to maximize organ functioning and minimize long-term side effects.
Type of QI	Process
Calculation	<u>Numerator</u>: Patients who had surgery only (with/without lymphadenectomy) or radiotherapy only. <u>Denominator</u>: Patients with clinical stage I or II disease who received treatment with curative intent (surgery or radiotherapy or the combination of both) with or without chemotherapy/targeted therapy. <u>Exclusions</u>: none
Target	80-85%
Data source	- Belgian Cancer Registry (BCR): incidence years 2009 – 2014 - IMA data
Technical definition	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1) Treatments: surgery with curative intent (IMA, Table 38 – Table 47), radiotherapy with curative intent (IMA, Table 48), chemotherapy (IMA, Table 54), targeted therapy (IMA, Table 55), lymphadenectomy (IMA, Table 46 and Table 55)
Risk adjustment	None (process indicator)
Limitations	Inevitably, some patients will need additional treatment after surgery e.g. based on final pathological stage. It can be expected that about 15-20% of patients receive RT after surgery. If this proportion is higher, this can be due to suboptimal staging and/or surgery.
Subgroup analyses	- Patients with pathological stage I-II versus pathological stage III - Anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx) - Age at diagnosis - Gender
Sensitivity analyses	Distribution of treatment schemes by age, clinical stage and anatomic site Distribution of treatment schemes radiotherapy or surgery together with systemic therapy, by anatomic site Distribution of treatment schemes radiotherapy and surgery, by anatomic site
Benchmarking	By centre of main treatment

Flowchart
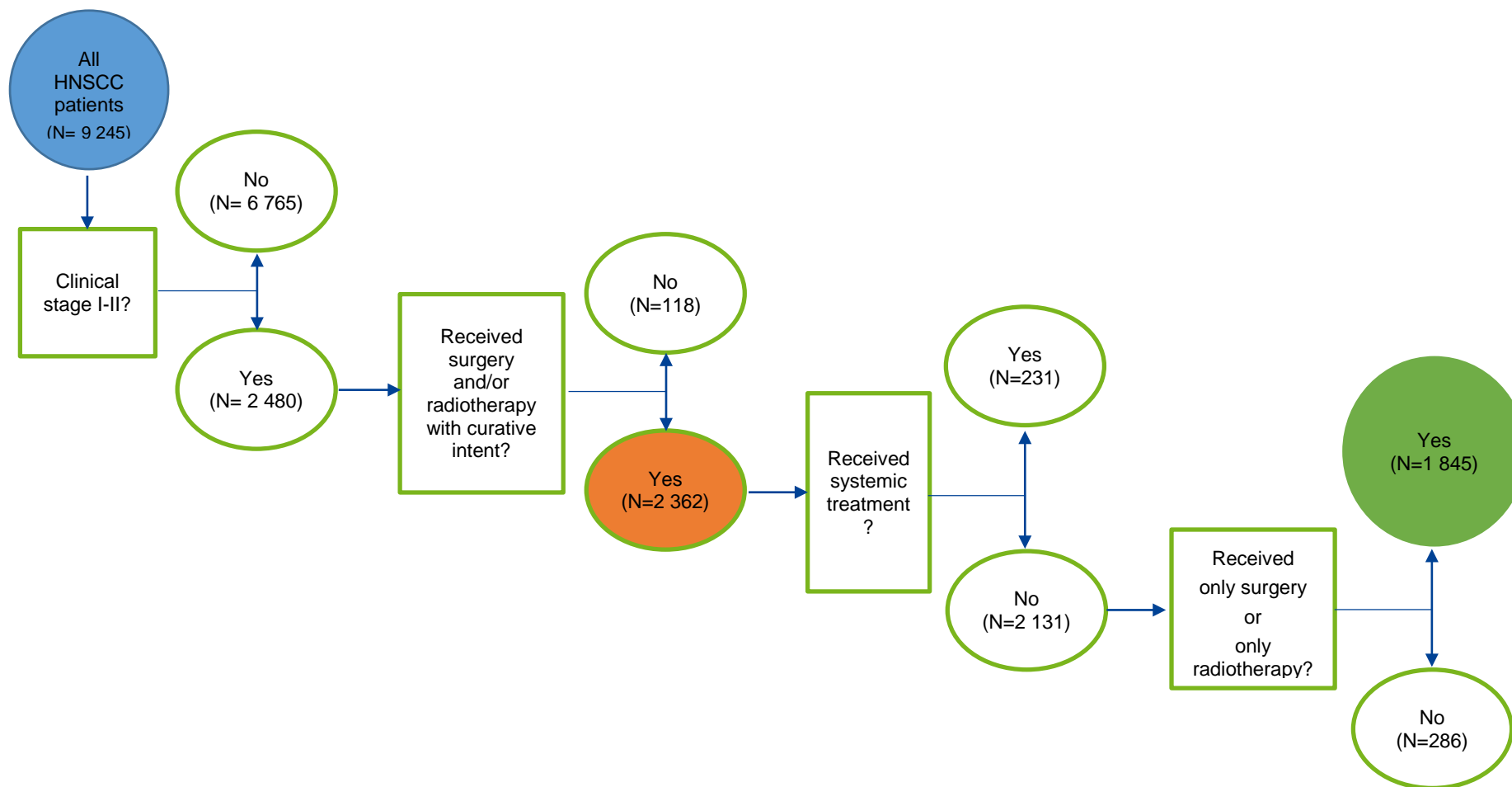
Results

Table 110 – Proportion of patients with early stage (cI or cII) HNSCC treated with a single-modality approach, by patient and tumour characteristics (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	2 362	1 845	78.1
Surgery only		850	36.0
RT only		995	42.1
Anatomic site			
Oral cavity	773	540	69.9
Oropharynx	388	253	65.2
Hypopharynx	94	56	59.6
Larynx	1 107	996	90.0
Gender			
Males	1 775	1 404	79.1
Females	587	441	75.1
Age at diagnosis			
<50 years	251	175	69.7
50-59 years	732	555	75.8
60-69 years	757	587	77.5
70-79 years	423	349	82.5
80+ years	199	179	89.9
Pathological stage*			
I-II	806	648	80.4
III	90	37	41.1

*Note: * Among the total of 2 362 patients, 1 172 were not surgically treated and another 294 had a pathological stage IV or X (missing).*
Source: BCR – IMA

Table 111 – Distribution of treatment schemes for patients with early stage (cI or cII) HNSCC who were treated with radiotherapy and/or surgery, by age, clinical stage and anatomic site (2009-2014)

Characteristics	Total	Surgery only	Surg < RT	RT < Surg	RT + LND	RT only
	N	N (%)	N (%)	N (%)	N (%)	N (%)
Overall	2 131	850 (39.9)	252 (11.8)	15 (0.7)	19 (0.9)	995 (46.7)
Age at diagnosis						
<50 years	207	112 (54.1)	31 (15.0)	0 (0.0)	1 (0.5)	63 (30.4)
50-59 years	650	270 (41.5)	89 (13.7)	1 (0.2)	5 (0.8)	285 (43.8)
60-69 years	684	260 (38.0)	84 (12.3)	6 (0.9)	7 (1.0)	327 (47.8)
70-79 years	395	130 (32.9)	38 (9.6)	5 (1.3)	3 (0.8)	219 (55.4)
80+ years	195	78 (40.0)	10 (5.1)	3 (1.5)	3 (1.5)	101 (51.8)
Clinical stage						
I	1 275	605 (47.5)	86 (6.7)	7 (0.5)	12 (0.9)	565 (44.3)
II	856	245 (28.6)	166 (19.4)	8 (0.9)	7 (0.8)	430 (50.2)
Anatomic site						
Oral cavity	703	507 (72.1)	156 (22.2)	1 (0.1)	6 (0.9)	33 (4.7)
Oropharynx	325	107 (32.9)	65 (20.0)	3 (0.9)	4 (1.2)	146 (44.9)
Hypopharynx	60	7 (11.7)	3 (5.0)	0 (0.0)	1 (1.7)	49 (81.7)
Larynx	1 043	229 (22.0)	28 (2.7)	11 (1.1)	8 (0.8)	767 (73.5)

LND: lymph node dissection
Source: BCR – IMA

Table 112 – Distribution of treatment schemes for patients with early stage (cI or cII) HNSCC who were treated with radiotherapy and/or surgery together with systemic therapy, by anatomic site (2009-2014)

Characteristics	Total	syst < Surg	syst<surg<syst	syst/RT<surg	syst/RT	RT<surg<syst	surg<syst	surg<syst/RT
	N	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)
Overall	231	6 (2.6)	1 (0.4)	1 (0.4)	138 (59.7)	4 (1.7)	9 (3.9)	72 (31.2)
Anatomic site								
Oral cavity	70	4 (5.7)	1 (1.4)	0 (0.0)	7 (10.0)	2 (2.9)	7 (10.0)	49 (70.0)
Oropharynx	63	2 (3.2)	0 (0.0)	1 (1.6)	47 (74.6)	0 (0.0)	0 (0.0)	13 (20.6)
Larynx	64	0 (0.0)	0 (0.0)	0 (0.0)	55 (85.9)	2 (3.1)	2 (3.1)	5 (7.8)
Hypopharynx	34	0 (0.0)	0 (0.0)	0 (0.0)	29 (85.3)	0 (0.0)	0 (0.0)	5 (14.7)

Source: BCR – IMA

Table 113 – Distribution of treatment schemes for patients with early stage (cI or cII) HNSCC who were treated with radiotherapy and surgery, by anatomic site (2009-2014)

Characteristics	Total	RT<surg	Surg<RT	RT + LND
	N	N (%)	N (%)	N (%)
Overall	286	15 (5.2)	252 (88.1)	19 (6.6)
Anatomic site				
Oral cavity	163	1 (0.6)	156 (95.7)	6 (3.7)
Oropharynx	72	3 (4.2)	65 (90.3)	4 (5.6)
Larynx	47	11 (23.4)	28 (59.6)	8 (17.0)
Hypopharynx	4	0 (0.0)	3 (75.0)	1 (25.0)

LND: lymph node dissection
Source: BCR – IMA

International comparison

Table 114 – Single modality approach in clinical stage I-II HNSCC patients - International results (2009-2014)

Author	Period covered	country	Results
Petersen et al., 2018[95]	1991 - 2010	The Netherlands	During the 20-year study period, 91 (20.6%) patients with stage I-II **hypopharyngeal** SCC received surgery alone (total laryngectomy or local surgery); the majority of patients (n=279, 63.3%) were treated with radiotherapy alone. Taken together, 83.9% of the study population received a single modality treatment.
Gogarty et al., 2017[94]	1997 - 2007	Ireland	During the study period, 237 (59.7%) patients with stage I-II **oral cavity** SCC received surgery alone while only 66 (16.6%) patients were treated with radiotherapy alone. In total, 76.3% of patients with early stage oral cavity SCC received a single modality treatment.
Gourin et al., 2014[93]	2004 - 2007	US (Surveillance, Epidemiology, and End Results (SEER) database)	The study was confined to elderly (i.e. 66 years and older) patients with stage I-II **laryngeal** SCC: 587 (35.0%) patients received RT alone. Only a minority (n=36, 2.1%) of patients with stage II laryngeal SCC received surgery alone. The number of patients with stage I laryngeal SCC who received surgery was not reported to comply with the SEER–Medicare data use (i.e. cells with <11 observations). Hence, at least 37% of the patients included in the database received a single modality approach.

Appendix 7.2.2. Proportion of patients with T4a laryngeal cancer who underwent total laryngectomy (SX-1)

Documentation sheet

Title	Proportion of patients with non-metastatic T4a laryngeal cancer who underwent total laryngectomy
Rationale	Recommendations in the KCE guideline:[23] In patients with advanced oropharyngeal, hypopharyngeal or laryngeal cancer, organ and function-sparing procedures are recommended. However, in patients with T4a laryngeal cancer, total laryngectomy should be considered.
Type of QI	Process
Calculation	Numerator: number of patients who had a total laryngectomy Denominator: number of patients with non-metastatic T4a laryngeal cancer who received any kind of treatment
Target	≥80% (due to medical contra-indications some patients are not eligible)
Data sources	- Belgian Cancer Registry (BCR): incidence years 2009 – 2014 - IMA data
Technical definitions	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1) Total laryngectomy: Information on the type of surgical procedure was retrieved from pathology reports available at the Belgian Cancer Registry.

Title	Proportion of patients with non-metastatic T4a laryngeal cancer who underwent total laryngectomy
	Treatments: surgery with curative intent (IMA, Table 38 – Table 47), radiotherapy with curative (IMA, Table 48) or palliative (IMA, Table 49) intent, chemotherapy (IMA, Table 54), targeted therapy (IMA, Table 55)
Risk adjustment	None (process indicator)
Limitations	Many patients could not be included in the denominator because TNM information was not specific enough.
Subgroup analyses	By age at diagnosis and gender
Sensitivity analyses	None
Benchmarking	Main treatment centre

Flowchart
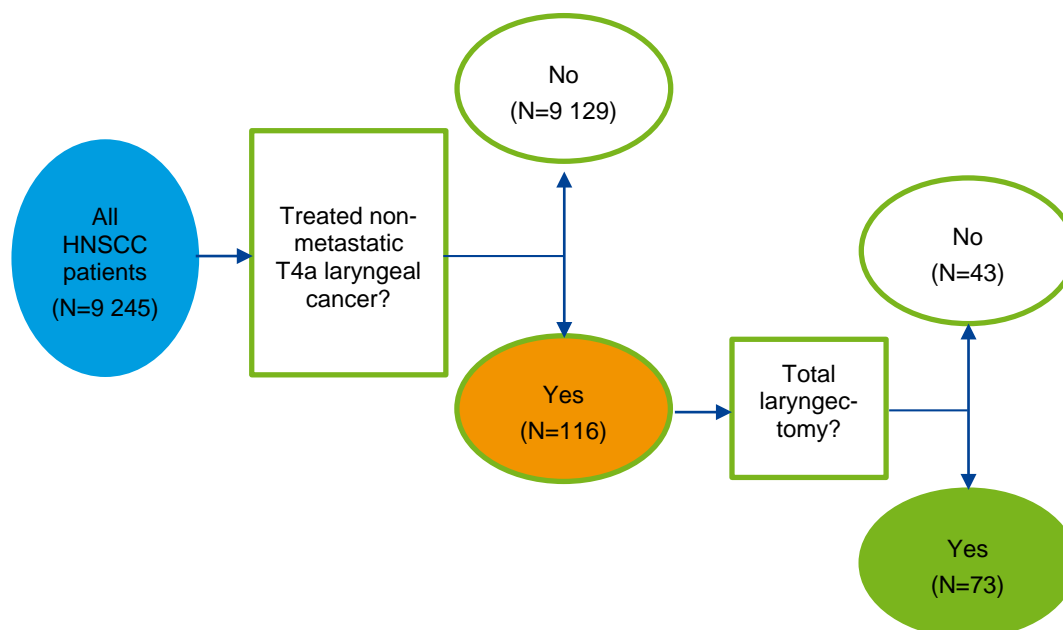
Results

Table 115 – Proportion of patients with non-metastatic T4a laryngeal cancer who underwent total laryngectomy, by patient characteristics (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	116	73	62.9
Gender			
Males	104	68	65.4
Females	12	5	41.7
Age at diagnosis			
<50 years	6	2	33.3
50-59 years	39	22	56.4
60-69 years	43	29	67.4
70-79 years	20	15	75.0
80+ years	8	5	62.5

Source: BCR – IMA

International comparison

Table 116 – Total laryngectomy in patients with laryngeal cancer - International results

Author	Period covered	Country	Results
Eskander et al., 2017[140]	2003-2010	Ontario, Canada	Overall, 14.8% (n=448/3 034) of all laryngeal and hypopharyngeal cancer patients (from the Ontario Cancer Registry) had a laryngectomy procedure (partial, total, or pharyngolaryngectomy). This proportion was significantly higher among males (15.5% vs. 10.8% in females, p<0.01), younger age groups (16.9% for age 18-54 years vs. 10.6% for age ≥75 years, p<0.01), those in the lowest income quintile (16.9% vs. 14.1% in the highest quintile, p=0.04).
Choi et al., 2016[97]	2000-2012	Republic of Korea	Among the 89 patients diagnosed with T4a laryngeal cancer with thyroid cartilage invasion in seven institutions, 53 (59.6%) were initially treated with total laryngectomy and 36 (40.4%) with larynx-preservation therapy. The two groups did not differ significantly in baseline characteristics, except that the clinical N1 classification was more likely to be treated with total laryngectomy (88.2%).
Timmermans et al., 2016[98]	1991-2010	The Netherlands	Among the 3 794 T3 (n=2 072) and T4 (n=1 722) laryngeal cancer cases, 30.9% (n=1 172) received total laryngectomy as primary treatment modality; this proportion was higher in males (32.5%), glottis subsite (35.7%), and T4N0* category (50.4%). Total laryngectomy as primary treatment modality decreased from approximately 48% to 15% during the study period.
Gourin et al., 2011[96]	1990-2009	Maryland, USA	Among the 1 981 laryngeal cancer cases**, total laryngectomy, including laryngo-pharyngectomy, was the most common surgical procedure and was performed in 72% of all patients; this proportion decreased from 75% in 1990-1999 to 69% in 2000-2009 (p=0.0004).

*Of the total of 1 722 patients with T4 laryngeal cancer, there were 1 208 with unspecified T4 cases, 489 with T4a cases, and 25 with T4b cases (of which 4 underwent a total laryngectomy); ** The Maryland HSCRC database contains no information on stage of disease, grade, subtype, or survival.*

Appendix 7.2.3. Timeliness postoperative radiotherapy (RT-1)

Documentation sheet

Title	Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was completed within thirteen weeks after surgery
Rationale	The KCE guideline recommended to start postoperative (chemo)radiotherapy as early as possible, i.e. within 6 weeks after surgery, and to complete the adjuvant treatment within 11-13 weeks after surgery.[23] Since the publication of the guideline, more evidence was published, supporting the importance of a timely start of postoperative RT.[141] More precisely, initiating postoperative radiation therapy (PORT) later than six weeks after surgery was associated with decreased survival in HNSCC patients, but no survival benefit was obtained with starting PORT earlier than this six week time frame.[141] While other guidelines and audit reports (cf. infra) concentrated on the start of postoperative radiotherapy within six weeks after surgery, it was opted to focus here on the fact that radiotherapy was completed within thirteen weeks after surgery, as the experts indicated that the total treatment time is the most important aspect. Therefore, when post-operative RT cannot be started within six weeks (e.g. in case of post-operative complications), this can be compensated during the RT course so that all fractions are given within thirteen weeks after surgery.
Type of QI	Process
Calculation	<u>Numerator</u>: patients for whom adjuvant radiotherapy was completed within thirteen weeks after surgery <u>Denominator</u>: patients with HNSCC treated with primary surgery and adjuvant radiotherapy (i.e. started up to six months after surgery)
Target	≥ 90%
Data source	- Belgian Cancer Registry (BCR): incidence years 2009 – 2014 - IMA data
Technical definition	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1) Radiotherapy with curative intent: billing codes (IMA) in Table 48 Definition adjuvant radiotherapy: started within six months after surgery Surgery with curative intent: billing codes (IMA) in Table 38 – Table 47 (Surgery is defined with the algorithm to define surgery with curative intent (see section 3.3.2.2).
Risk adjustment	None (process indicator)
Limitations	- Based on the RIZIV – INAMI licensing codes mentioned in the IMA data, it is impossible to distinguish the centre of a satellite radiotherapy unit from the centre of the main radiation oncology department. In case radiotherapy was performed in a satellite unit, the patient was assigned to the centre of the corresponding main radiation oncology department. - Start date of radiotherapy is not always available in the IMA – AIM database; for these cases the start date of radiotherapy is estimated based on the simulation date. If also the simulation date is not available, the start date is estimated based on the end date and duration of the series of similar patients for whom the start date is available in the IMA-database.

Title	**Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was completed within thirteen weeks after surgery**
	- Another limitation is that it is impossible to distinguish patients who completed the whole RT scheme from patients who received their RT fractions within the recommended time frame after surgery, but who stopped their treatment before it was completed (when an RT-scheme is stopped, the fee for the whole scheme is billed, even when not all fractions are given). Consequently, rather to use the terminology 'radiotherapy was completed within thirteen weeks after surgery', we will use 'radiotherapy was ended within thirteen weeks after surgery' in the description of results.
Subgroup analyses	- Anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx) - Combined stage - Age at diagnosis - Gender - WHO performance status - Comorbidities - RT referral status: no referral for RT (i.e. centre where adjuvant RT was given is the same as the centre where surgery with curative intent was performed) vs. referred for RT (i.e. centre where adjuvant RT was given is different from the centre where surgery with curative intent was performed)
Sensitivity analyses	Timeliness post-operative RT (i.e. started within six weeks after surgery versus seven weeks) Radiotherapy ended within fourteen or fifteen weeks after surgery
Benchmarking	Main treatment centre and RT centre

Flowchart
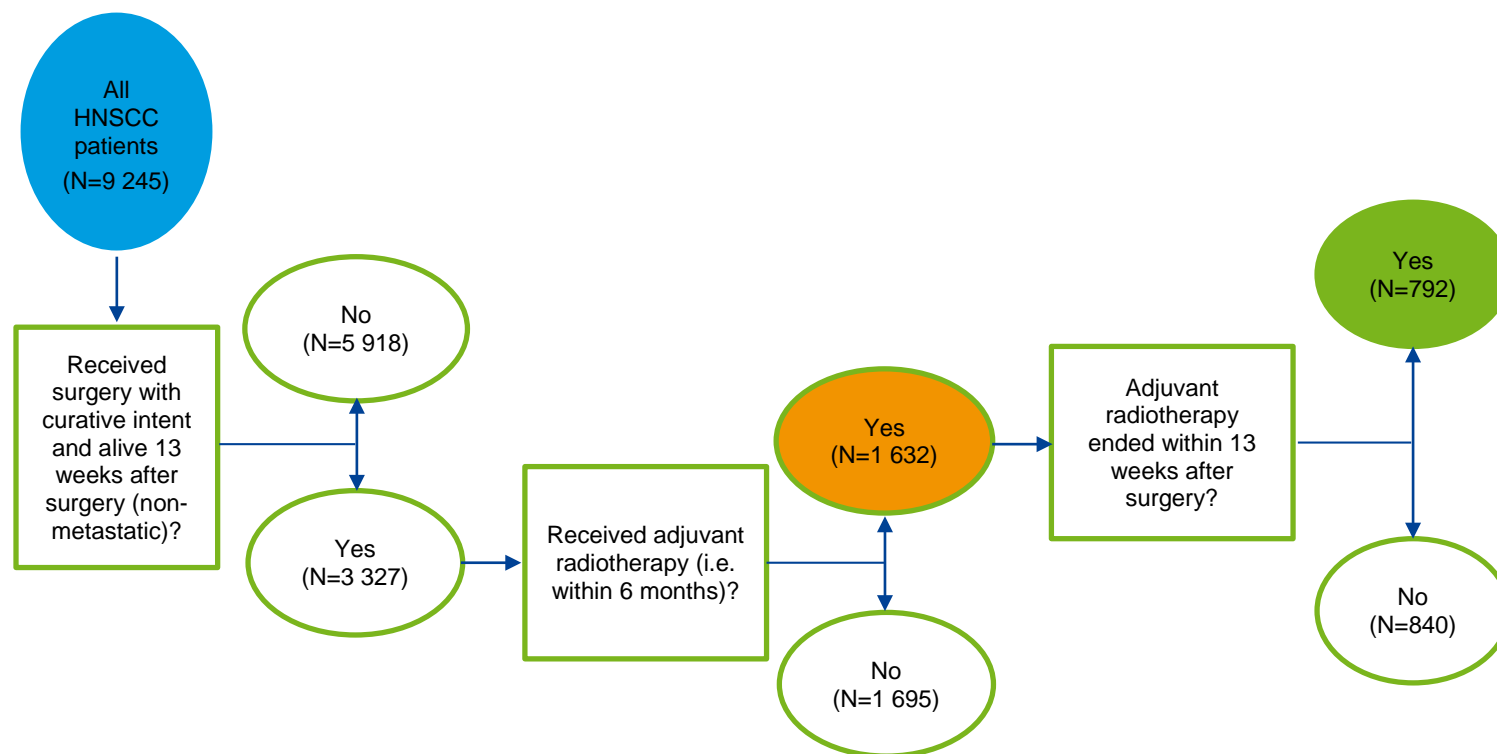
Results

Table 117 – Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was ended within thirteen weeks after surgery, by patient and tumour characteristics (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	1 632	792	48.5
Anatomic site			
Oral cavity	860	388	45.1
Oropharynx	377	221	58.6
Hypopharynx	116	55	47.4
Larynx	279	128	45.9
Gender			
Male	1 202	587	48.8
Female	430	205	47.7
Age at diagnosis			
<50 years	220	116	52.7
50-59 years	624	292	46.8
60-69 years	520	262	50.4
70-79 years	207	96	46.4
80+ years	61	26	42.6
Combined stage			
I	147	68	46.3
II	214	110	51.4
III	292	161	55.1
IVA/B	899	411	45.7
X	4	4	100.0
WHO performance status			
0 – Asymptomatic	288	153	53.1
1 – Symptomatic but completely ambulatory	1 047	486	46.4

Characteristics	Denominator	Numerator	Proportion (%)
2 – Symptomatic, <50% in bed during the day	28	17	60.7
3 – Symptomatic, >50% in bed, but not bedbound	8	2	25.0
4 – Bedbound	2		0.0
Missing	259	134	51.7
Adapted Charlson Comorbidity Index*			
0	971	481	49.5
1-2	626	299	47.8
3-4	12	5	41.7
>4	-	-	-
RT referral status			
No referral for RT	909	472	51.9
Referral for RT	723	320	44.3

* For 23 patients it was impossible to define the Adapted Charlson Comorbidity Index.
Source: BCR – IMA – MZG

Table 118 – Proportion of patients with HNSCC who were treated with postoperative RT in whom RT was started within 6 or 7 weeks after surgery and ended within 13-15 weeks (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Time interval between date of surgery until start date RT			
6 weeks	1 632	556	34.1
7 weeks	1 632	864	52.9
Time interval between date of surgery until end date RT			
13 weeks	1 632	792	48.5
14 weeks	1 632	1 028	63.0
15 weeks	1 632	1 170	71.7

Source: BCR – IMA

Table 119 – Time (in days) from date of surgery to start and end of adjuvant radiotherapy, by anatomic site

Characteristics	N	Q1	Median	Q3
Time (in days) from date of surgery to start of adjuvant radiotherapy				
Overall	1 632	40	49	65
Anatomic site				
Oral cavity	860	42	50	70
Oropharynx	377	35	45	59
Hypopharynx	116	41	49	63
Larynx	279	40	49	64
Time (in days) from date of surgery to end of adjuvant radiotherapy				
Overall	1 632	84	92	108
Anatomic site				
Oral cavity	860	85	93	112
Oropharynx	377	79	89	102
Hypopharynx	116	85	92.5	106
Larynx	279	82	93	107

Source: BCR – IMA

Figure 29 – Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was ended within thirteen weeks after surgery, by main treatment centre (2009-2014)
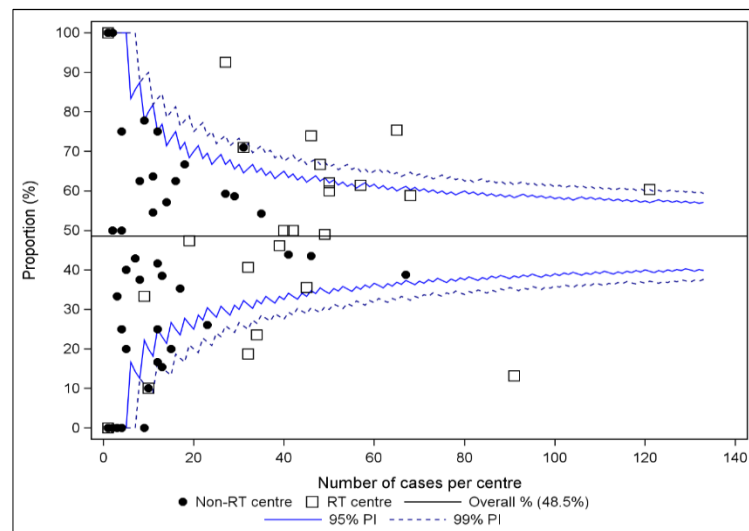
Note: 85 centres reported in the funnel plot; the 24 RT centres are represented by a square (2 RT centres have no patients assigned to them based on the algorithm to select the main treatment centre and are consequently not reported in the funnel plot).
Source: BCR – IMA

Figure 30 – Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was started within six weeks after surgery, by main treatment centre (2009-2014)
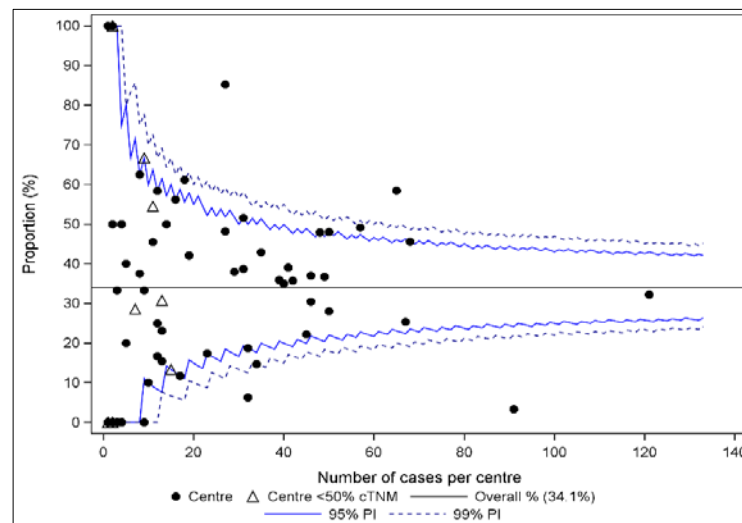
Note: 85 centres reported in the funnel plot; 10 centres reported for less than 50% of their patients clinical stages; they are represented by an open triangle.
Source: BCR – IMA

Figure 31 – Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was started within six weeks after surgery, by radiotherapy centre (2009-2014)
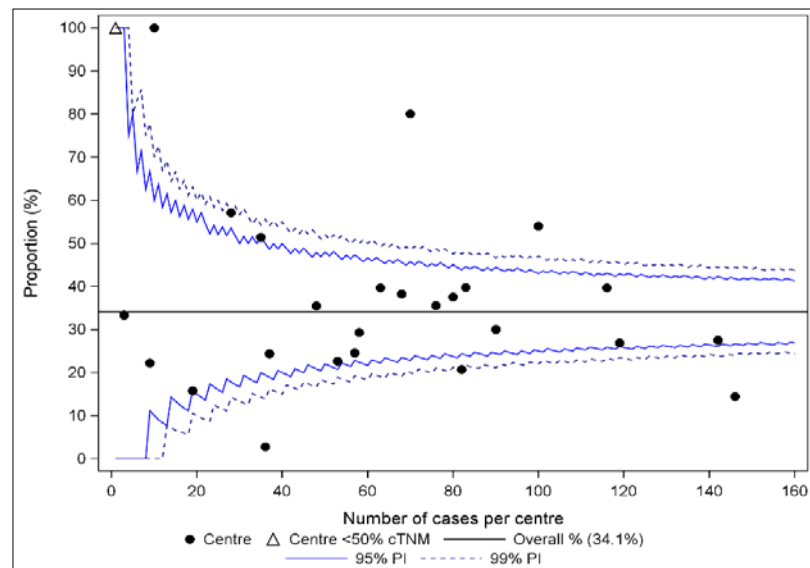
Note: 26 centres reported in the funnel plot; 3 patients were not included in the analyses as they could not be assigned to a RT centre, but their data are included in the analyses for the overall result; 1 centre which reported for less than 50% of its assigned patients cTNM to the BCR, is represented by an open triangle.
Source: BCR – IMA

Figure 32 – Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was started within six weeks after surgery, by main treatment centre (2009-2014)
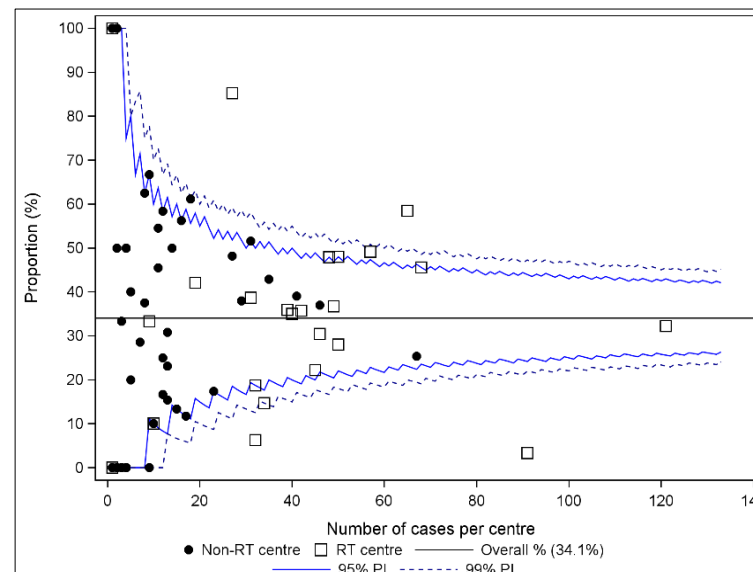
Note: 85 centres reported in the funnel plot; the 24 RT centres are represented by a square.
Source: BCR – IMA

Figure 33 – Time from date of surgery (with curative intent) to the end date of adjuvant radiotherapy, by main treatment centre (2009-2014)

Oral cavity – 74 centres
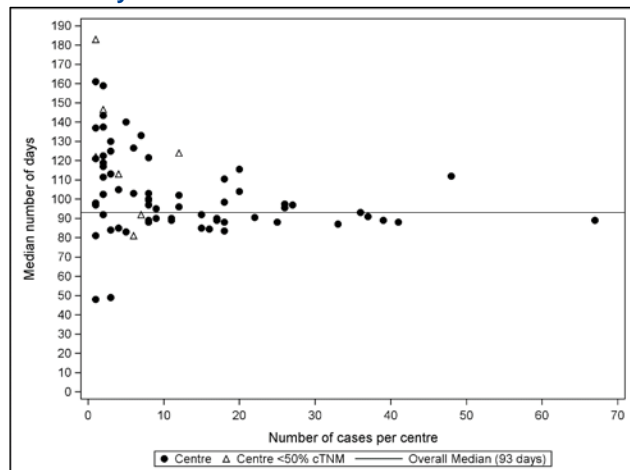
Oropharynx – 71 centres
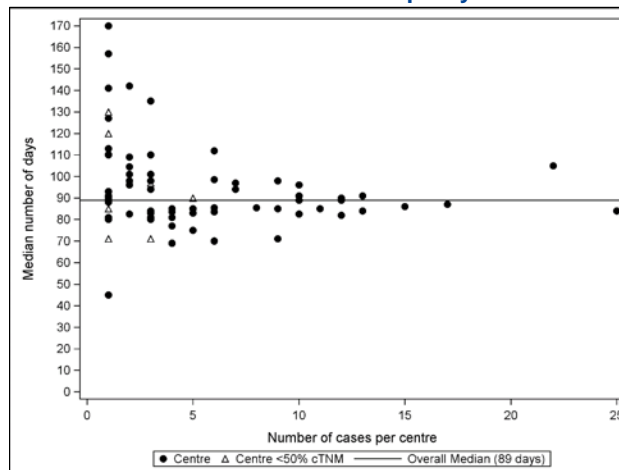
Hypopharynx – 27 centres
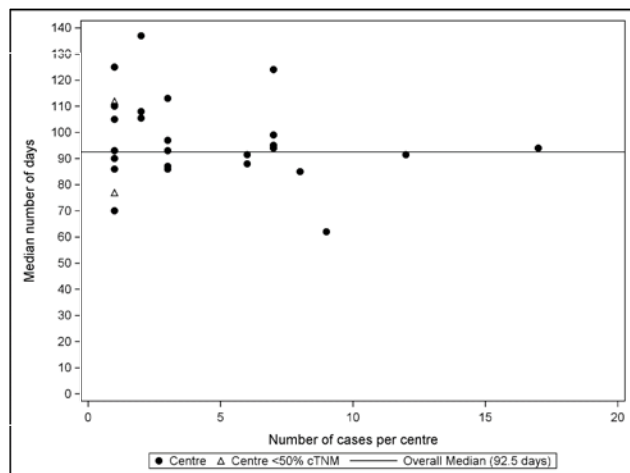
Larynx – 49 centres
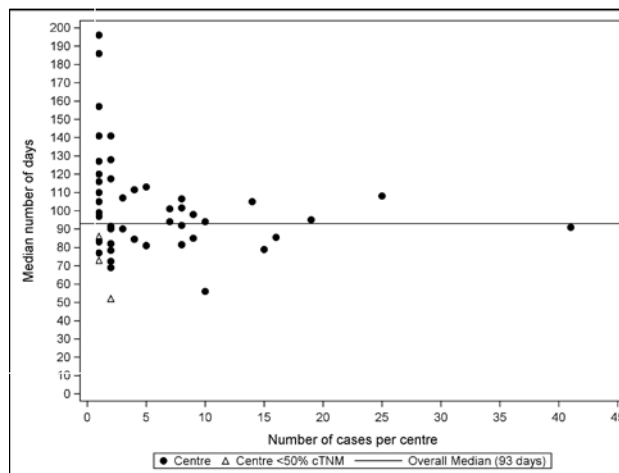
Note: Centres which reported for less than 50% of their assigned patients cTNM to the BCR, are represented by an open triangle (i.e. oral cavity and oropharynx: 8 centres, hypopharynx: 2 centres and larynx: 3 centres).
Source: BCR – IMA

Figure 34 – Time from date of surgery (with curative intent) to the end date of adjuvant radiotherapy, by RT centre (2009-2014)

Oral cavity – 25 centres
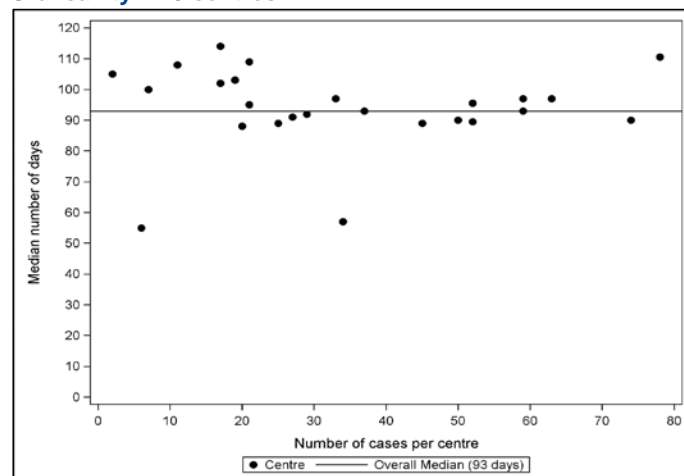
Oropharynx – 24 centres
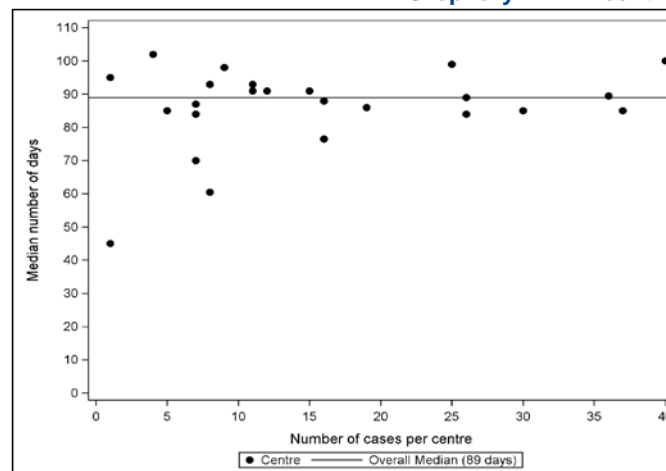
Hypopharynx – 20 centres
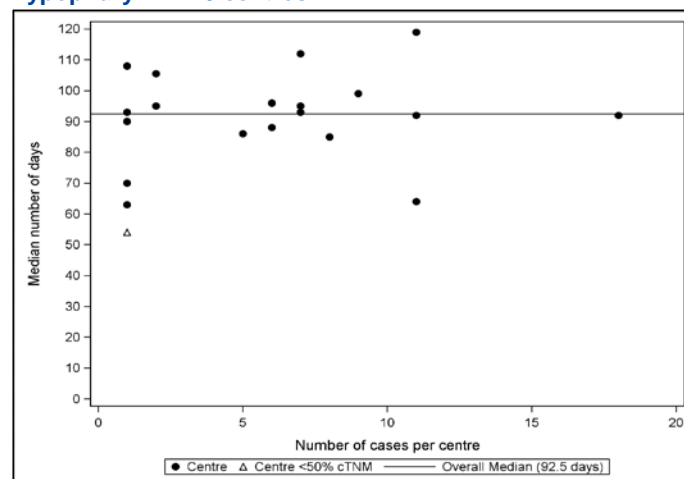
Larynx – 24 centres
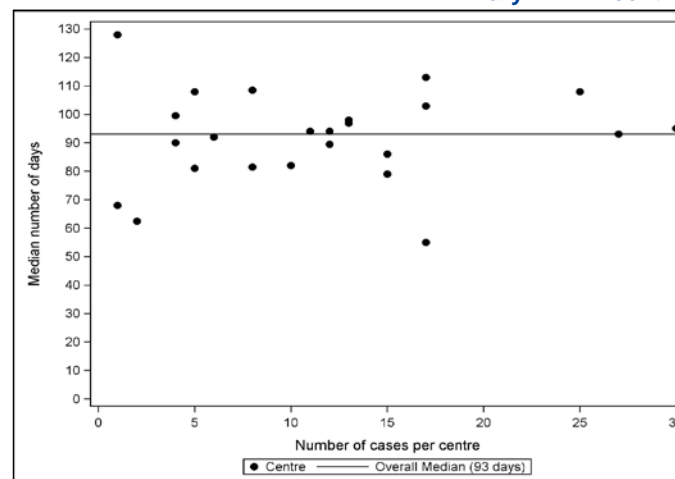
Note: centres which reported for less than 50% of their assigned patients cTNM to the BCR, are represented by an open triangle; two patients with oral cavity SCC and one patient with laryngeal SCC were not included in the analyses as they could not be assigned to a RT centre, but their data are included in the analyses for the overall result.

Source: BCR – IMA

International comparison

Table 120 – Time interval between surgery and adjuvant radiotherapy in HNSCC patients - International results

Author	Period covered	Country	Results
Graboyes et al., 2017[100]	2006-2014	USA	The study cohort was composed of 47 273 patients. Globally, 55.7% of patients failed to start PORT within six weeks of surgery, and this percentage increased over time (52.9% of patients in 2006 vs. 58.7% of patients in 2014; p<0.001).
Health and Social Care Information Centre, Tenth Annual Report, 2015[87]	November 2013 - October 2014	England and Wales	During the 1-year audit period, of 4 267 patients treated with surgery, 872 had postoperative radiotherapy (PORT), equating to 20.4%. The median interval between surgery and start of adjuvant radiotherapy was fifty days for all anatomic sites (seven weeks). Over six Annual Reports, timely access to radiotherapy has not significantly improved. Huge variability in the time to start RT was observed between cancer networks, from a median of 39 days (5.5 weeks) to a median of 76 days (11 weeks).

Appendix 7.2.4. Primary chemoradiotherapy for locally-advanced non-metastatic disease (RT-2)

Documentation sheet

Title	Proportion of medically fit patients with locally-advanced (stage III and IV) non-metastatic HNSCC treated with primary RT, who received concomitant platinum-based chemotherapy
Rationale	When radiation therapy is selected as primary treatment, concomitant platinum-based chemoradiation is now considered to be the standard first-line therapy to treat medically fit patients with locally-advanced HNSCC.[101] Large randomized trials and meta-analyses have proved that platinum-based concomitant chemoradiotherapy regimens provide significantly higher response rates than radiotherapy alone.[142, 143] Yet, the advantages from the simultaneous combination of chemotherapy and radiotherapy are at the expense of acute and late toxicity.[23]
	The KCE guideline recommends primary concomitant platinum-based chemoradiotherapy in medically fit patients with locally-advanced (stage III and IV) SCC of the head and neck (except in patients with T4a laryngeal cancer). Further, the authors of the guideline considered the combination of radiotherapy and cetuximab as an alternative for those patients who do not tolerate platinum-based chemoradiotherapy.[23]
Type of QI	Process
Calculation	Numerator: All patients who received concomitant platinum-based chemoradiotherapy
	Denominator: All medically fit (WHO score 0-1) patients with locally-advanced (stage III and IV) non-metastatic (M0) SCC of the head and neck treated with primary RT
	Exclusions:
	T4a laryngeal cancer
Target	≤ 70 years: 75-80%
	> 70 years: no target specified

Title	**Proportion of medically fit patients with locally-advanced (stage III and IV) non-metastatic HNSCC treated with primary RT, who received concomitant platinum-based chemotherapy**
Data sources	• Belgian Cancer Registry (BCR): incidence years 2009 –2014 • IMA data
Technical definitions	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1) Radiotherapy with curative intent: billing codes (IMA) in Table 48 Platinum-based chemotherapy: billing codes (IMA) in Table 54 Systemic therapy, including chemotherapy and targeted therapy (for sensitivity analysis): billing codes (IMA) in Table 54 and Table 55 Concomitant chemotherapy is defined as chemotherapy that started from seven days before the start of radiotherapy to any time during the RT series; in the principal analyses only this chemotherapy is included. Induction chemotherapy is defined as chemotherapy that started between 120 days and 7 days before the start of radiotherapy (limited to sensitivity analyses) Systemic therapy that started after the end of radiotherapy is not included (in any analyses).
Risk adjustment	None (process indicator)
Limitations	'Medically fit' is defined using WHO Performance status, which is not for all included patients available in the database
Subgroup analyses	- Anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx) - Clinical stage - Age at diagnosis (cf. supra: patients older than seventy years old are often not eligible for platinum-based chemoradiotherapy) - Gender - Adapted Charlson Comorbidity Index

Sensitivity analyses	- Concomitant versus induction CT, for all HNSCC and by anatomic site
	- Systemic therapy agents used
	    o Platinum-based chemo (i.e. cisplatinum or carboplatinum, the latter with or without 5FU)
	    o Cetuximab only
	    o Non-platinum-based chemo (no platinum-based, no targeted therapy)
	    o Chemo (platinum- and/or non-platinum-based) + Cetuximab

Benchmarking	Centre of main treatment

Flowchart

Results

Table 121 – Proportion of medically fit patients with locally-advanced stage (stage III and IV) non-metastatic HNSCC treated with primary RT who received concomitant platinum-based chemotherapy, by patient and tumour characteristics (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	2 350	1 241	52.8
Anatomic site			
Oral cavity	236	101	42.8
Oropharynx	1 156	630	54.5
Hypopharynx	556	306	55.0
Larynx	402	204	50.7
Gender			
Males	1 834	984	53.7
Females	516	257	49.8
Age at diagnosis			
<50 years	215	136	63.3
50-59 years	854	509	59.6
60-69 years	865	480	55.5
70-79 years	308	109	35.4
80+ years	108	7	6.5
Adapted Charlson Comorbidity Index *			
0	1 405	800	56.9
1-2	718	357	49.7
3-4	134	48	35.8
>4	34	8	23.5
Clinical stage			
III	601	279	46.4
IVA/IVB	1 749	962	55.0

* For 59 patients it was impossible to define the Adapted Charlson Comorbidity Index.
Source: BCR – IMA – MZG

Table 122 – Proportion of medically fit patients with locally-advanced stage (stage III and IV) non-metastatic HNSCC treated with primary RT who received concomitant systemic therapy, by type of agent(s) (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Concomitant systemic therapy agents			
- Any concomitant systemic therapy	2 350	1 407	59.9
o Platinum-based chemo (i.e. cisplatinum or carboplatinum, the latter with or without 5FU)	2 350	1 231	52.4
o Cetuximab only	2 350	164	7.0
o Non-platinum-based chemo (no platinum-based, no targeted therapy)	2 350	1	0.0
o Chemo (platinum- and/or non-platinum-based) + Cetuximab	2 350	11	0.5

Source: BCR – IMA

Table 123 – Proportion of medically fit patients with locally-advanced stage (stage III and IV) non-metastatic HNSCC treated with primary RT who received concomitant platinum-based chemotherapy vs. induction platinum-based chemotherapy, by anatomic site (2009-2014)

Characteristics	Patients	Concomitant		Induction	
	N	N	%	N	%
Overall	**2 350**	**1 241**	**52.8**	**479**	**20.4**
Oral cavity	236	101	42.8	69	29.2
Oropharynx	1 156	630	54.5	237	20.5
Hypopharynx	556	306	55.0	125	22.5
Larynx	402	204	50.7	48	11.9

Source: BCR – IMA

International comparison

Table 124 – Primary chemoradiotherapy in locally-advanced HNSCC - International results

Author	Period covered	Country	Results
Doornaert et al., 2015[144]	2014-2015	The Netherlands	In the Netherlands, HNSCC patients are referred to one of the eight head and neck reference centres that work in collaboration with thirteen radiotherapy centres (members of the National Platform RT HNC 'Landelijk Platform Radiotherapie Hoofdhals Tumoren'). These RT centres were surveyed to determine how T3 laryngeal carcinoma are currently being managed in the Netherlands. Twelve centres completed the survey reporting the systematic use of primary radiotherapy for the primary tumour, with or without concomitant chemotherapy/biological therapy, and with or without upfront neck dissection when deemed necessary. CRT was dedicated to voluminous T3N0 and most T3N+ tumours, but there were some differences between the centres in the use of chemotherapy (cisplatin three-weekly or weekly; with or without age limit of seventy years) and the dose-fractionation schemes. Above the age of seventy years, three centres reported that they generally combine radiotherapy with cetuximab when the patient is very fit. The other centres did not report combined therapy for this age group.
Health and Social Care Information Centre, Tenth Annual Report, 2015[87]	November 2013 - October 2014	England and Wales	During the 1-year audit period, 607 cases of laryngeal cancer had sufficient staging information to be recorded as advanced. Of these 607 patients, 38.9% received surgery as first active treatment, 16.5% received chemoradiotherapy and 12.7% underwent radiotherapy. Among patients with T3 glottic cancer, 25% received CRT, 21.6% received only RT and 29.9% were operated. In patients with T4 glottic cancer, these proportions were respectively 6.3%, 8% and 52.3%.

Appendix 7.2.5. Neck imaging after primary (chemo)radiotherapy (LN-1)

Documentation sheet

Title	**Proportion of patients with node-positive HNSCC treated with primary (chemo)radiotherapy, in whom a diagnostic evaluation of the neck with PET(/CT) or DW-MRI was performed not earlier than three months after completion of primary therapy**
Rationale	The role of image-guided surveillance as compared with planned neck dissection in the treatment of HNSCC patients with advanced nodal disease who have received (chemo)radiotherapy for primary treatment has largely been investigated. In two meta-analyses, PET-CT in patients with HNSCC who have received (chemo)radiotherapy have shown high negative predictive values (95%),[104, 105] therefore suggesting that imaging assessments of the patients' response to therapy may result in fewer operations (and complications) and be more cost-effective, which is consistent with results from a recent randomized controlled trial.[103] Recently, results from the prospective multicenter ECLYPS (Combined FDG PET(/CT) Imaging in Response Evaluation After Radiochemotherapy in Patients With Locally Advanced HNSCC) study suggested that FDG-PET(/CT) surveillance using standardized reporting criteria twelve weeks after concurrent chemoradiotherapy is reliable in locally advanced HNSCC except for late manifesting residual disease, which may require an additional surveillance scan at one year after treatment to be detected.[145] According to the KCE guidelines, in node-positive HNSCC patients treated with primary (chemo)radiotherapy, a diagnostic evaluation of the neck with PET(/CT) or DW-MRI should be performed not earlier than three months after completion of primary (chemo)radiotherapy.[23]

Title	Proportion of patients with node-positive HNSCC treated with primary (chemo)radiotherapy, in whom a diagnostic evaluation of the neck with PET(/CT) or DW-MRI was performed not earlier than three months after completion of primary therapy
Type of QI	Process
Calculation	Numerator: All patients in whom a diagnostic evaluation of the neck with PET(/CT) or (DW-)MRI was performed between ten and sixteen weeks after completion of the primary therapy
	Denominator: All patients with node-positive SCC of the head and neck treated with primary (chemo)radiotherapy ((C)RT)
	CRT also includes targeted therapy (e.g. cetuximab) combined with RT
	Date of imaging is considered acceptable between ten and sixteen weeks after completion of primary (chemo)radiotherapy
	Exclusion: patients deceased within sixteen weeks after completion of (C)RT
Target	80%
Data sources	- Belgian Cancer Registry (BCR): incidence years 2009 – 2014
	- IMA data
Technical definitions	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1)
	Diagnostic procedures: PET(/CT) (IMA, Table 28), (DW-)MRI (IMA, Table 26 and Table 27)
	Treatments: radiotherapy with curative intent (IMA, Table 48), chemotherapy (IMA, Table 54), targeted therapy (IMA, Table 55)
Risk adjustment	None (process indicator)
Limitations	No specific codes for MRI, DW not identifiable from other MRI techniques
Subgroup analyses	- Anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx)
	- Clinical stage
	- Age at diagnosis
	- Gender
Sensitivity analyses	- Per time period: the evidence underlying this recommendation was only published between 2006 and 2008, so the data of the earlier years should be interpreted with caution as implementation of a recommendation does take some time;
	- Per time frame (after the end of treatment):
	o PET(/CT) or (DW-)MRI before 10 weeks
	o PET(/CT) or (DW-)MRI between 10 and 24 weeks
	o PET(/CT) or (DW-)MRI between 24 weeks and 1 year
Benchmarking	By centre of main treatment

Flowchart

Results

Table 125 – Proportion of patients with node-positive HNSCC treated with primary (chemo)radiotherapy, in whom a diagnostic evaluation of the neck with PET(/CT) or (DW-)MRI was performed between ten and sixteen weeks after completion of the primary therapy, by patient and tumour characteristics (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	2 171	709	32.7
Anatomic site			
Oral cavity	193	52	26.9
Oropharynx	1 116	374	33.5
Hypopharynx	492	183	37.2
Larynx	370	100	27.0
Gender			
Males	1 698	550	32.4
Females	473	159	33.6
Age at diagnosis			
<50 years	230	82	35.7
50-59 years	844	268	31.8
60-69 years	785	278	35.4
70-79 years	242	63	26.0
80+ years	70	18	25.7
Clinical stage			
III	368	118	32.1
IVA/B	1 737	567	32.6
IVC	66	24	36.4

Source: BCR – IMA

Table 126 – Sensitivity analyses per time period and time frames (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Time period			
2009-2011	1 035	287	27.7
2012-2014	1 136	422	37.1
Time frames			
PET(/CT) or (DW-)MRI before 10 weeks*	2 171	171	7.9
PET(/CT) or (DW-)MRI within 10-24 weeks	2 171	907	41.8
PET(/CT) or (DW-)MRI after 24 weeks (but before 1 year)	2 171	190	8.8
No follow-up with PET(/CT) or (DW-)MRI within 1 year	2 171	903	41.6

* Five patients who had a PET(/CT) or (DW-)MRI in this time frame (i.e. before 10 weeks) had an additional PET(/CT) or (DW-)MRI after 24 weeks (but before 1 year).
Source: BCR – IMA

Appendix 7.2.6. Elective neck dissection in cN0M0 squamous cell carcinoma of the head and neck (LN-2)

Documentation sheet

Title	Proportion of surgically treated patients with HNSCC and cN0M0/x with any T stage (except T1 glottic cancer), who underwent elective neck dissection
Rationale	Although evidence is limited, there are indications that elective lymph node dissection of the neck may result in improved disease-free survival. Data on an approach of watchful waiting are insufficiently reassuring to consider this treatment option as safe. Therefore the following recommendations were given in the KCE guideline[23]:
	Management of the neck lymph nodes should follow the **same treatment principles** as those applied for the primary tumour (e.g. if the primary tumour is surgically treated, a neck dissection should be performed). In patients with oropharyngeal, hypopharyngeal and supraglottic cancer, **bilateral elective neck treatment** (surgery or radiotherapy) is recommended. However, in small lateralised cancers, unilateral neck treatment can be considered. In patients with **early (stage I or II) glottic cancer, neck treatment can be omitted**, with the exception of supraglottic extension.
Type of QI	Process
Calculation	Numerator: patients who underwent elective lymph node dissection of the neck
	Denominator: patients with cN0M0/x, any T HNSCC who underwent primary surgery
	Exclusions: T1 glottic cancer

Title	**Proportion of surgically treated patients with HNSCC and cN0M0/x with any T stage (except T1 glottic cancer), who underwent elective neck dissection**
Target	≥90%
Data source	• Belgian Cancer Registry (BCR): incidence years 2009 – 2014 • IMA data
Technical definition	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1) Glottic cancer: ICD-10 code C32.0, C32.8, C32.9 (BCR) Treatments: surgery with curative intent (IMA, Table 38 – Table 47), lymph node dissection of the neck (IMA, Table 46 and Table 55)
Risk adjustment	None (process indicator)
Limitations	None
Subgroup analyses	- Anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx) - Clinical stage - Age at diagnosis - Gender - WHO performance status & comorbidities - Incidence year
Sensitivity analyses	Elective neck dissection within two weeks versus within six weeks after surgery of the primary tumour (Table 129)
Benchmarking	By centre of main treatment

Flowchart
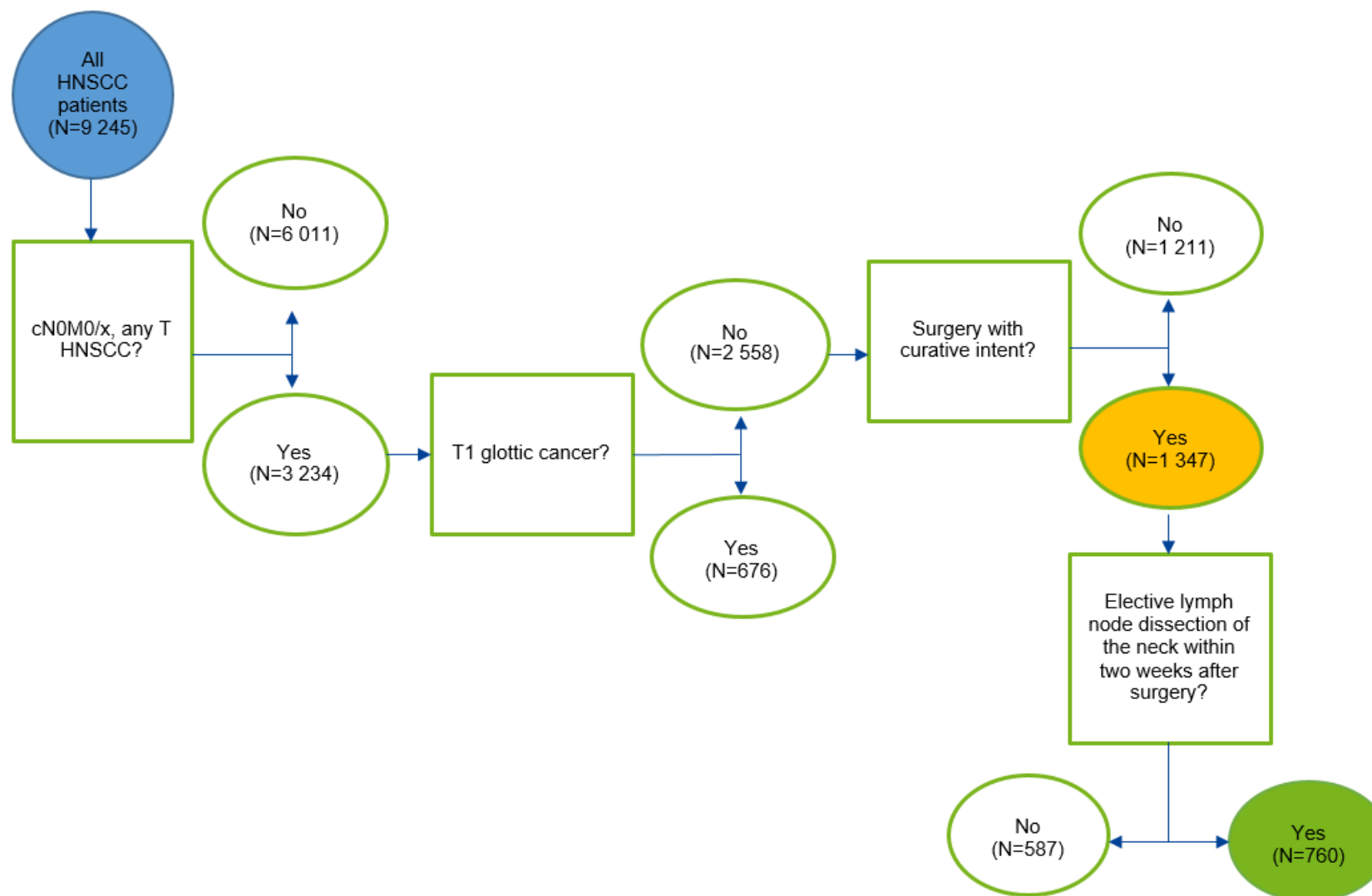
Results

Table 127 – Proportion of surgically treated HNSCC patients with cN0M0/x with any T stage (except T1 glottic cancer), who underwent elective neck dissection (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Overall	1 347	760	56.4
Anatomic site			
Oral cavity	869	500	57.5
Oropharynx	210	91	43.3
Hypopharynx	29	21	72.4
Larynx	239	148	61.9
Gender			
Males	922	567	61.5
Females	425	193	45.4
Age at diagnosis			
<50 years	175	103	58.9
50-59 years	449	282	62.8
60-69 years	414	240	58.0
70-79 years	207	100	48.3
80+ years	102	35	34.3
WHO performance status			
0 – Asymptomatic	285	157	55.1
1 – Symptomatic but completely ambulatory	915	534	58.4
2 – Symptomatic, <50% in bed during the day	24	11	45.8
3 – Symptomatic, >50% in bed, but not bedbound	8	4	50.0
4 – Bedbound	1	0	0.0
Missing	114	54	47.4
Adapted Charlson Comorbidity Index *			
0	817	413	50.6

Characteristics	Denominator	Numerator	Proportion (%)
1-2	484	329	68.0
3-4	16	12	75.0
>4	-	-	-
Clinical stage			
I	500	194	38.8
II	430	274	63.7
III	100	75	75.0
IVA/IVB	242	184	76.0
X (missing)	75	33	44.0
Incidence year			
2009	207	114	55.1
2010	207	112	54.1
2011	220	129	58.6
2012	240	129	53.8
2013	218	122	56.0
2014	255	154	60.4

* For thirty patients it was impossible to define the Adapted Charlson Comorbidity Index. Source: BCR – IMA – MZG

Table 128 – Proportion of surgically treated HNSCC patients with cN0M0/x with any T stage (except T1 glottic cancer) who had adjuvant RT, but no elective neck dissection (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Adjuvant RT	587	173	29.5
No adjuvant RT	587	414	70.5

Source: BCR – IMA

Table 129 – Proportion of surgically treated HNSCC patients with cN0M0/x with any T stage (except T1 glottic cancer) who underwent elective neck dissection within two weeks versus within six weeks after surgery of the primary tumour (2009-2014)

Characteristics	Denominator	Numerator	Proportion (%)
Until two weeks after surgery	1 347	760	56.4
Until six weeks after surgery	1 347	833	61.8

Source: BCR – IMA

Table 130 – Proportion of surgically treated HNSCC patients with cN0M0/x with any T stage (except T1 glottic cancer) who underwent elective neck dissection, by gender, anatomic site and clinical stage (2009-2014)

	ALL			FEMALES			MALES		
	Denominator	Numerator	Proportion (%)	Denominator	Numerator	Proportion (%)	Denominator	Numerator	Proportion (%)
Oral cavity	**869**	**500**	**57.5**	**308**	**141**	**45.8**	**561**	**359**	**64.0**
I	391	166	42.5	160	48	30.0	231	118	51.1
II	268	202	75.4	85	58	68.2	183	144	78.7
III	35	28	80.0	11	10	90.9	24	18	75.0
IVA/B	122	84	68.9	33	19	57.6	89	65	73.0
X	53	20	37.7	19	6	31.6	34	14	41.2
Oropharynx	**210**	**91**	**43.3**	**70**	**25**	**35.7**	**140**	**66**	**47.1**
I	91	24	26.4	30	8	26.7	61	16	26.2
II	87	44	50.6	30	13	43.3	57	31	54.4
III	9	7	77.8	2	1	50.0	7	6	85.7
IVA/B	9	9	100.0	2	2	100.0	7	7	100.0
X	14	7	50.0	6	1	16.7	8	6	75.0
Hypopharynx	**29**	**21**	**72.4**	**7**	**4**	**57.1**	**22**	**17**	**77.3**
I	6	1	16.7	2		0.0	4	1	25.0
II	6	4	66.7	1	1	100.0	5	3	60.0
III	4	4	100.0	2	2	100.0	2	2	100.0
IVA/B	12	11	91.7	1		0.0	11	11	100.0
X	1	1	100.0	1	1	100.0			
Larynx	**239**	**148**	**61.9**	**40**	**23**	**57.5**	**199**	**125**	**62.0**

	ALL			FEMALES			MALES		
	Denominator	Numerator	Proportion (%)	Denominator	Numerator	Proportion (%)	Denominator	Numerator	Proportion (%)
I	12	3	25.0	7	1	14.3	5	2	40.0
II	69	24	34.8	15	8	53.3	54	16	29.6
III	52	36	69.2	7	5	71.4	45	31	68.9
IVA/B	99	80	80.8	10	8	80.0	89	72	80.9
X	7	5	71.4	1	1	100.0	6	4	66.7

Source: BCR – IMA

Table 131 – Proportion of surgically treated HNSCC patients with cN0M0/x with any T stage (except T1 glottic cancer) who underwent elective neck dissection, by adapted Charlson Comorbidity Index, anatomic site and clinical stage (2009-2014)

	Adapted Charlson Comorbidity Index *								
	0			1-2			3-4		
	Denominator	Numerator	Proportion (%)	Denominator	Numerator	Proportion (%)	Denominator	Numerator	Proportion (%)
Oral cavity	**547**	**280**	**51.2**	**284**	**208**	**73.2**	**9**	**6**	**66.7**
I	276	110	39.9	100	55	55.0	2	1	50.0
II	154	109	70.8	104	87	83.7	3	3	100.0
III	17	15	88.2	17	13	76.5	-	-	-
IVA/B	67	37	55.2	48	42	87.5	3	2	66.7
X	33	9	27.3	15	11	73.3	1	0	0.0
Oropharynx	**144**	**59**	**41.0**	**63**	**31**	**49.2**	**2**	**1**	**50.0**
I	63	15	23.8	26	8	30.8	2	1	50.0
II	61	31	50.8	25	13	52.0	-	-	-
III	3	3	100.0	6	4	66.7	-	-	-
IVA/B	6	6	100.0	3	3	100.0	-	-	-
X	11	4	36.4	3	3	100.0	-	-	-
Hypopharynx	**13**	**9**	**69.2**	**15**	**11**	**73.3**	**1**	**1**	**100.0**
I	5	1	20.0	1	0	0.0	-	-	-

	Adapted Charlson Comorbidity Index *								
	0			1-2			3-4		
	Denominator	Numerator	Proportion (%)	Denominator	Numerator	Proportion (%)	Denominator	Numerator	Proportion (%)
II	2	2	100.0	4	2	50.0	-	-	-
III	1	1	100.0	3	3	100.0	-	-	-
IVA/B	5	5	100.0	6	5	83.3	1	1	100.0
X	-	-	-	1	1	100.0	-	-	-
Larynx	**113**	**65**	**57.5**	**122**	**79**	**64.8**	**4**	**4**	**100.0**
I	4	1	25.0	8	2	25.0	-	-	-
II	43	15	34.9	26	9	34.6	-	-	-
III	21	16	76.2	30	19	63.3	1	1	100.0
IVA/B	43	32	74.4	53	45	84.9	3	3	100.0
X	2	1	50.0	5	4	80.0	-	-	-

For thirty patients it was impossible to define the Adapted Charlson Comorbidity Index.
Source: BCR – IMA – MZG

International comparison

Table 132 – Elective neck dissection in cN0M0 squamous cell carcinoma of the head and neck - International results

Author	Period covered	Country	Results
Kuo et al., 2016[106]	1998-2006	US (Surveillance, Epidemiology, and End Results (SEER) database)	The study was confined to cN0 patients with SCC in the **oral cavity**. Among the patients who had known clinical lymph node status (n=6 147), 79% had cN0 disease. The rate of neck dissection was 63.9% in the cN0 cohort and 98.3% in the cN1cohort.
Health and Social Care Information Centre, Tenth Annual Report, 2014[87]	November 2013 - October 2014	England and Wales	In the database, there were 614 cases with T1-T2 N0 **tongue tumours**. The most common surgical procedure in this group was excision lesion of the tongue (n=258) or partial glossectomy (n=268). In 216 (41%) of these patients a neck dissection was recorded.

Appendix 7.3. Safety of care

Appendix 7.3.1. Post-treatment mortality (G-1)

Documentation sheet

Title	Proportion of patients with HNSCC who die within 30 days of treatment with curative intent
Rationale	Careful selection of the right treatment for the right patient is essential to achieve the best outcomes. For example, providing aggressive surgery to a patient with comorbidities puts this patient at a high risk of having postoperative complications and even death. In addition, treatment should be provided in the safest way as possible. The 30-day mortality captures both the selection of patients and the safety of the treatment provided.
Type of QI	Outcome

Calculation	**Indicator A: 30 day post-operative mortality**
	  Numerator: Number of patients who died within 30 days after surgery
	  Denominator: All patients with HNSCC who received surgery with curative intent
	Indicator B: 30 day post-radiotherapy mortality
	  Numerator: Number of patients who died within 30 days after the last day of radiotherapy
	  Denominator: All patients with HNSCC who received radiotherapy with curative intent
	Exclusions (for indicator A and B): combined stage IVC

Target	< 5%
Data sources	• Belgian Cancer Registry (BCR): incidence years 2009 –2014 • Crossroads Bank of Social Security (Kruispuntbank van de Sociale Zekerheid (KSZ) - Banque Carrefour de la Sécurité Sociale (BCSS)) for mortality data (vital status of patients diagnosed with cancer): follow-up until 14 December 2017 • IMA data for subgroup analyses
Technical definition	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1) Treatments: surgery with curative intent (IMA, Table 38 – Table 47), radiotherapy with curative intent (IMA, Table 48)
Risk adjustment	None
Limitations	There are residual confounding factors (e.g. SES background) for which no adjustments can be made.
Subgroup analyses	- Anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx) - Combined stage - Age at diagnosis - Gender - WHO performance status - Comorbidities - Previous inpatient bed days
Sensitivity analyses	- 60 and 90-day mortality - Logistic regression model with the following factors as covariates: anatomic site, age at diagnosis, gender, comorbidity, WHO performance status, combined stage and previous inpatient bed days

Title	Proportion of patients with HNSCC who die within 30 days of treatment with curative intent
Benchmarking	By main treatment centre

Flowchart 30-day post-operative mortality
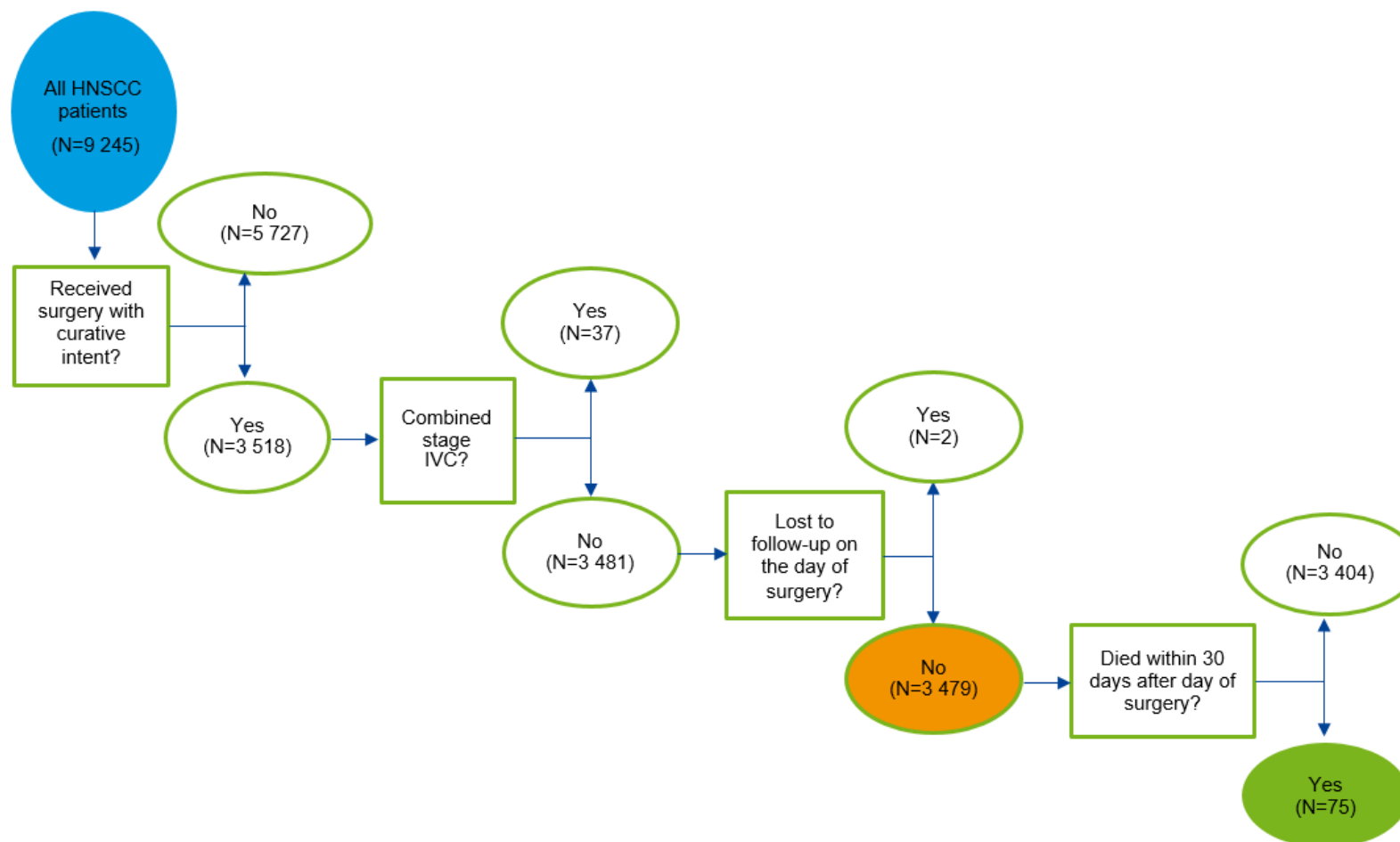
Flowchart 30-day post-radiotherapy mortality
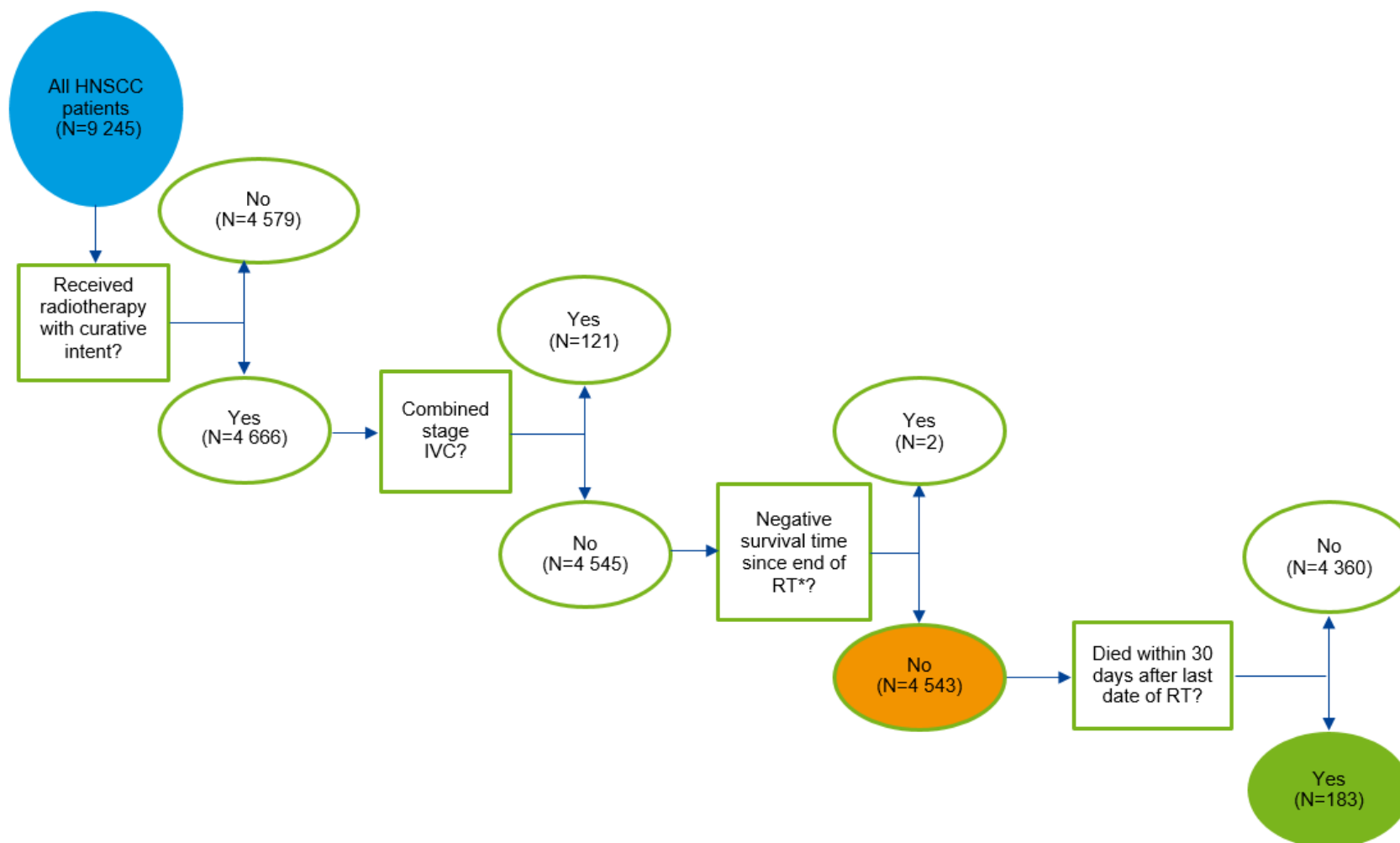
This is a limitation of using administrative databases.

Results

Table 133 – Proportion of patients with HNSCC who die within 30, 60 and 90 days after surgery with curative intent, by patient and tumour characteristics (2009-2014)

Characteristics	N at risk	30-day post-operative mortality		60-day post-operative mortality		90-day post-operative mortality	
		N of deaths	% (95% CI)	N of deaths	% (95% CI)	N of deaths	% (95% CI)
Overall	3 479	75	2.2 (1.7, 2.6)	120	3.4 (2.8, 4.1)	159	4.6 (3.9, 5.3)
Anatomic site							
Oral cavity	1 943	39	2.0 (1.4, 2.7)	63	3.2 (2.5, 4.1)	91	4.7 (3.8, 5.7)
Oropharynx	627	13	2.1 (1.1, 3.2)	25	4.0 (2.6, 5.6)	30	4.8 (3.2, 6.5)
Hypopharynx	151	2	1.3 (0.0, 3.3)	5	3.3 (0.7, 6.6)	8	5.3 (2.0, 9.3)
Larynx	758	21	2.8 (1.7, 4.0)	27	3.6 (2.2, 4.9)	30	4.0 (2.6, 5.4)
Gender							
Male	2 456	63	2.6 (2.0, 3.2)	98	4.0 (3.2, 4.8)	126	5.1 (4.3, 6.0)
Female	1 023	12	1.2 (0.6, 1.9)	22	2.2 (1.3, 3.1)	33	3.2 (2.2, 4.3)
Age at diagnosis (years)							
<50	438	1	0.2 (0.0, 0.7)	2	0.5 (0.0, 1.1)	4	0.9 (0.2, 1.8)
50-59	1 172	20	1.7 (1.0, 2.5)	31	2.6 (1.8, 3.6)	39	3.3 (2.3, 4.4)
60-69	1 075	21	2.0 (1.2, 2.8)	36	3.3 (2.3, 4.5)	46	4.3 (3.1, 5.5)
70-79	537	22	4.1 (2.4, 5.8)	34	6.3 (4.3, 8.4)	48	8.9 (6.5, 11.4)
80 +	257	11	4.3 (1.9, 7.0)	17	6.6 (3.9, 9.7)	22	8.6 (5.4, 12.1)
WHO performance status							
0 – Asymptomatic	618	8	1.3 (0.5, 2.3)	12	1.9 (1.0, 3.1)	16	2.6 (1.5, 3.9)
1 – Symptomatic but completely ambulatory	2 030	38	1.9 (1.3, 2.5)	62	3.1 (2.3, 3.8)	82	4.0 (3.2, 4.9)
2 – Symptomatic, <50% in bed during the day	54	1	1.9 (0.0, 5.6)	7	13 (5.6, 22.2)	11	20.4 (11.1, 31.5)
3 – Symptomatic, >50% in bed, but not bedbound	22	3	13.6 (0.0, 27.3)	4	18.2 (4.5, 36.4)	6	27.3 (9.1, 45.5)
4 – Bedbound	6	1	16.7 (0.0, 50.0)	1	16.7 (0.0, 50.0)	1	16.7 (0.0, 50.0)

Characteristics	N at risk	30-day post-operative mortality		60-day post-operative mortality		90-day post-operative mortality	
		N of deaths	% (95% CI)	N of deaths	% (95% CI)	N of deaths	% (95% CI)
Missing	749	24	3.2 (2.0, 4.5)	34	4.5 (3.1, 6.1)	43	5.7 (4.1, 7.5)
Combined stage							
I	1 046	8	0.8 (0.3, 1.3)	12	1.1 (0.6, 1.8)	18	1.7 (1.0, 2.6)
II	509	7	1.4 (0.4, 2.6)	13	2.6 (1.4, 3.9)	17	3.3 (2.0, 4.9)
III	446	10	2.2 (0.9, 3.8)	14	3.1 (1.6, 4.9)	19	4.3 (2.5, 6.3)
IV A/B	1 167	39	3.3 (2.3, 4.4)	62	5.3 (4.0, 6.6)	81	6.9 (5.5, 8.4)
X (unknown)	311	11	3.5 (1.6, 5.8)	19	6.1 (3.5, 9.0)	24	7.7 (4.8, 10.9)
Previous inpatient bed days							
None	629	5	0.8 (0.2, 1.6)	15	2.4 (1.3, 3.7)	20	3.2 (1.9, 4.6)
1-5 days	1 837	28	1.5 (1.0, 2.1)	42	2.3 (1.6, 3.0)	56	3.0 (2.3, 3.9)
6-15 days	648	18	2.8 (1.5, 4.2)	34	5.2 (3.5, 7.1)	46	7.1 (5.2, 9.1)
>15 days	365	24	6.6 (4.1, 9.3)	29	7.9 (5.2, 10.7)	37	10.1 (7.1, 13.4)
Adapted Charlson Comorbidity Index							
0	2 079	16	0.8 (0.4, 1.2)	34	1.6 (1.1, 2.2)	50	2.4 (1.8, 3.1)
1-2	1 098	36	3.3 (2.3, 4.4)	51	4.6 (3.5, 5.9)	63	5.7 (4.4, 7.2)
3-4	198	15	7.6 (4.0, 11.6)	19	9.6 (5.6, 13.6)	25	12.6 (8.1, 17.2)
>4	43	8	18.6 (7.0, 30.2)	14	32.6 (18.6, 46.5)	17	39.5 (25.6, 53.5)
Missing	61	0	0.0	2	3.3 (0.0, 8.2)	4	6.6 (1.6, 13.1)

Source: BCR – IMA – MZG

Table 134 – Proportion of patients with HNSCC who die within 30, 60 and 90 days after radiotherapy with curative intent, by patient and tumour characteristics (2009-2014)

Characteristics	N at risk	30-day post-RT mortality		60-day post-RT mortality		90-day post-RT mortality	
		N of deaths	% (95% CI)	N of deaths	% (95% CI)	N of deaths	% (95% CI)
Overall	4 543	183	4.0 (3.5, 4.6)	250	5.5 (4.8, 6.2)	341	7.5 (6.8, 8.3)
Anatomic site							
Oral cavity	408	27	6.6 (4.4, 9.1)	38	9.3 (6.6, 12.3)	60	14.7 (11.3, 18.1)
Oropharynx	1 703	75	4.4 (3.5, 5.4)	98	5.8 (4.7, 6.9)	127	7.5 (6.2, 8.7)
Hypopharynx	770	38	4.9 (3.5, 6.5)	55	7.1 (5.3, 9.0)	74	9.6 (7.5, 11.7)
Larynx	1 662	43	2.6 (1.9, 3.4)	59	3.5 (2.7, 4.5)	80	4.8 (3.8, 5.9)
Gender							
Male	3 610	149	4.1 (3.5, 4.8)	198	5.5 (4.8, 6.2)	264	7.3 (6.5, 8.2)
Female	933	34	3.6 (2.5, 4.9)	52	5.6 (4.2, 7.1)	77	8.3 (6.5, 10.1)
Age at diagnosis (years)							
<50	416	5	1.2 (0.2, 2.4)	10	2.4 (1.0, 4.1)	17	4.1 (2.4, 6.0)
50-59	1 537	31	2.0 (1.4, 2.7)	48	3.1 (2.3, 4.0)	76	4.9 (3.9, 6.1)
60-69	1 583	79	5.0 (3.9, 6.1)	104	6.6 (5.4, 7.8)	136	8.6 (7.3, 10.0)
70-79	721	45	6.2 (4.6, 8.0)	54	7.5 (5.7, 9.4)	66	9.2 (7.1, 11.4)
80 +	286	23	8.0 (4.9, 11.2)	34	11.9 (8.4, 15.7)	46	16.1 (11.9, 20.3)
WHO performance status							
0 – Asymptomatic	726	21	2.9 (1.8, 4.1)	31	4.3 (2.9, 5.8)	45	6.2 (4.5, 8.0)
1 – Symptomatic but completely ambulatory	2 990	112	3.7 (3.1, 4.4)	152	5.1 (4.3, 5.9)	213	7.1 (6.2, 8.1)
2 – Symptomatic, <50% in bed during the day	97	11	11.3 (5.2, 17.5)	15	15.5 (8.2, 22.7)	19	19.6 (12.4, 27.8)
3 – Symptomatic, >50% in bed, but not bedbound	26	8	30.8 (15.4, 50.0)	8	30.8 (15.4, 50.0)	8	30.8 (15.4, 50.0)
4 – Bedbound	4	0	0.0	0	0.0	0	0.0
Missing	700	31	4.4 (3.0, 6.0)	44	6.3 (4.6, 8.1)	56	8.0 (6.0, 10.0)

Characteristics	N at risk	30-day post-RT mortality		60-day post-RT mortality		90-day post-RT mortality	
		N of deaths	% (95% CI)	N of deaths	% (95% CI)	N of deaths	% (95% CI)
Combined stage							
I	665	8	1.2 (0.5, 2.1)	13	2.0 (1.1, 3.0)	18	2.7 (1.5, 4.1)
II	557	12	2.2 (1.1, 3.4)	19	3.4 (2.0, 5.0)	23	4.1 (2.5, 5.9)
III	721	30	4.2 (2.8, 5.7)	36	5.0 (3.5, 6.7)	45	6.2 (4.6, 8.0)
IV A/B	2 167	114	5.3 (4.3, 6.2)	155	7.2 (6.1, 8.3)	215	9.9 (8.7, 11.2)
X (unknown)	433	19	4.4 (2.5, 6.5)	27	6.2 (4.2, 8.5)	40	9.2 (6.7, 12.0)
Previous inpatient bed days							
None	235	7	3.0 (0.9, 5.5)	9	3.8 (1.7, 6.4)	13	5.5 (3.0, 8.5)
1-5 days	2 435	60	2.5 (1.8, 3.1)	86	3.5 (2.8, 4.3)	108	4.4 (3.7, 5.3)
6-15 days	1 169	51	4.4 (3.3, 5.6)	64	5.5 (4.2, 6.8)	91	7.8 (6.2, 9.3)
>15 days	704	65	9.2 (7.1, 11.4)	91	12.9 (10.5, 15.5)	129	18.3 (15.5, 21.2)
Adapted Charlson Comorbidity Index							
0	2 747	60	2.2 (1.6, 2.7)	85	3.1 (2.5, 3.7)	122	4.4 (3.7, 5.2)
1-2	1 261	75	5.9 (4.7, 7.3)	103	8.2 (6.7, 9.7)	143	11.3 (9.6, 13.1)
3-4	262	25	9.5 (6.1, 13.4)	36	13.7 (9.5, 17.9)	47	17.9 (13.4, 22.5)
>4	73	17	23.3 (13.7, 32.9)	18	24.7 (15.1, 34.2)	18	24.7 (15.1, 34.2)
Missing	200	6	3.0 (1.0, 5.5)	8	4.0 (1.5, 7.0)	11	5.5 (2.5, 9.0)

Source: BCR – IMA – MZG

Table 135 – Estimated Odds Ratios (and 95% CI) for the 30-day post-operative mortality (2009-2014)

	30-day post-operative mortality	
Characteristics	OR (95% CI)	p-value
Anatomic site		0.43
Oral cavity	1.00	
Oropharynx	1.26 (0.65, 2.45)	
Hypopharynx	0.38 (0.09, 1.66)	
Larynx	0.85 (0.47, 1.53)	
Gender		0.03
Male	2.12 (1.08, 4.14)	
Female	1.00	
Age at diagnosis (years)		0.002
<50	1.00	
50-59	5.93 (0.78, 44.91)	
60-69	5.94 (0.78, 44.99)	
70-79	12.49 (1.64, 94.87)	
80 +	19.23 (2.39, 154.68)	
WHO performance status		0.11
0 – Asymptomatic	1.00	
1 – Symptomatic but completely ambulatory	1.34 (0.61, 2.97)	
2 – Symptomatic, <50% in bed during the day	0.37 (0.04, 3.22)	
3 – Symptomatic, >50% in bed, but not bedbound	4.27 (1.09, 16.74)	
Missing	1.93 (0.80, 4.67)	
Combined stage		0.009
I	1.00	
II	1.33 (0.46, 3.84)	

	30-day post-operative mortality	
Characteristics	OR (95% CI)	p-value
III	2.52 (0.95, 6.66)	
IV A/B	3.55 (1.59, 7.92)	
X (unknown)	3.39 (1.24, 9.26)	
Previous inpatient bed days		0.25
None	1.00	
1-5 days	1.32 (0.49, 3.60)	
6-15 days	1.59 (0.54, 4.68)	
>15 days	2.42 (0.81, 7.24)	
Adapted Charlson Comorbidity Index		<0.0001
0/missing	1.00	
1-2	3.21 (1.70, 6.05)	
3-4	6.36 (2.87, 14.09)	
>4	14.42 (4.89, 42.49)	

Source: BCR – IMA – MZG

Table 136 – Estimated Odds Ratios (and 95% CI) for the 30-day post-radiotherapy mortality (2009-2014)

	30-day post-operative mortality	
Characteristics	OR (95% CI)	p-value
Anatomic site		0.20
Oral cavity	1.00	
Oropharynx	0.79 (0.49, 1.28)	
Hypopharynx	0.89 (0.52, 1.52)	
Larynx	0.58 (0.34, 1.00)	
Gender		0.24
Male	1.27 (0.85, 1.90)	
Female	1.00	

Characteristics	30-day post-operative mortality	
	OR (95% CI)	p-value
Age at diagnosis (years)		<0.0001
<50	1.00	
50-59	1.54 (0.59, 4.01)	
60-69	3.91 (1.55, 9.83)	
70-79	5.03 (1.95, 13.02)	
80 +	7.20 (2.62, 19.73)	
WHO performance status		0.007
0 – Asymptomatic	1.00	
1 – Symptomatic but completely ambulatory	1.19 (0.72, 1.97)	
2 – Symptomatic, <50% in bed during the day	2.42 (1.06, 5.51)	
3 – Symptomatic, >50% in bed, but not bedbound	5.32 (1.90, 14.87)	
Missing	1.35 (0.70, 2.60)	
Combined stage		0.004
I	1.00	
II	1.62 (0.64, 4.10)	
III	2.73 (1.20, 6.22)	
IV A/B	3.76 (1.72, 8.23)	
X (unknown)	2.96 (1.18, 7.46)	
Previous inpatient bed days		0.05
None	1.00	
1-5 days	1.07 (0.14, 8.18)	
6-15 days	1.32 (0.17, 10.17)	
>15 days	1.96 (0.25, 15.17)	
Adapted Charlson Comorbidity Index		<0.0001

	30-day post-operative mortality	
Characteristics	OR (95% CI)	p-value
0	1.00	
1-2	1.94 (1.33, 2.83)	
3-4	2.64 (1.52, 4.61)	
>4	7.86 (3.99, 15.49)	
Missing	1.37 (0.15, 12.14)	

Source: BCR – IMA – MZG

International comparison

Table 137 – Post-treatment mortality in HNSCC patients - International results

Author	Period covered	Country	Results
West of Scotland Cancer Network, Audit Report, 2017[108]	April 2016 – March 2017	Scotland	Of the 459 HNSCC patients treated with **surgery with curative intent**, there were 4 deaths within 30 days and no additional deaths within 90 days, which represent 30- and 90-day mortality rates of 0.9%. For the 232 patients receiving radical **radiotherapy** treatment, two patients died within 30 and 90 days (mortality rates of 0.9%). Finally, among the 228 patients who received **chemoradiotherapy,** nobody died within 30 days but there were two deaths within 90 days (90-day mortality rate of 0.8%).
NHS Quality Improvement Scotland Scotland, 2016[107]	April 2014 – March 2015	Scotland	Of the 419 HNSCC patients treated with **surgery with curative intent**, all were still alive after 30 days. For those patients receiving radical **radiotherapy** treatment, three patients died within 30 days; this represents a mortality rate of 1.2%. Finally, two patients out of the four hundred treated with **chemoradiotherapy** died within 30 days (30-day mortality rate of 0.8%).
Health and Social Care Information Centre, Tenth Annual Report, 2015[87]	November 2013 - October 2014	England and Wales	Among the 4 200 HNSCC patients **treated with surgery***, 72 (1.7%) died within 30 days and 114 (2.7%) within 90 days. Among those who were treated with curative intent (N=3 407), 54 (1.6%) and 81 (2.4%) died within 30- and 90-days, respectively. Among the 2 699 patients who underwent **non-surgical treatment**** (radiotherapy, chemotherapy or chemoradiotherapy), there were 61 deaths within 30 days (2.3%) and 140 deaths within 90 days (5.2%). Among those who were treated with curative intent (N=1 814), 23 (1.3%) and 65 (3.6%) died within 30- and 90-days, respectively.
Tighe et al., 2014[109]	2009-2010 for Site A, 2009-2011 for Site B, 2010-2012 for Site C	UK	Among the 807 HNSCC patients treated with **surgery** with curative intent at three NHS hospitals, seventeen died within 30 days, resulting in a postoperative 30-day mortality of 2.1%.
Chen et al., 2010[110]	1996-2002	USA	Among the 19 326 patients aged ≥18 years with **advanced-stage laryngeal cancer** (stages III and IV), 773 patients (4.0%) died within 90 days of diagnosis. Patients who received nonsurgical therapy (CRT or RT) had a statistically significant increased risk of death (CRT and RT: HR=1.46, 95% CI=1.22 - 1.75 and RT alone: HR=1.20, 95% CI=1.01 - 1.43), compared to total laryngectomy.

* The surgical group included a small number of patients treated with palliative intent (0.7%); ** The non-surgical group included patients treated with palliative intent (10.2%).

Appendix 7.4.   Observed and relative survival

Appendix 7.4.1. *The 1, 2 and 5-year observed and relative survival after a diagnosis of SCC of the head and neck (G-2)*

Documentation sheet

Title	The 1, 2 and 5-year observed and relative survival after a diagnosis of head & neck SCC
Rationale	Treatment of any cancer aims to cure or at least to prolong survival and improve quality of life of the involved patient.
	Observed survival reflects the proportion of patients still alive at some specified time after the diagnosis of cancer. It considers deaths from all causes, cancer related and non-cancer related. Relative survival, on the contrary, is related to the excess mortality that can be attributed to the cancer under study and is expressed as a percentage. For instance, a relative survival proportion of 50% indicates that the all-cause survival probability for patients who were diagnosed with cancer is only half of the probability in a comparable group sampled from the general population with the same characteristics (e.g. age, gender, residence and calendar year).
	This indicator reflects the effectiveness of a country's healthcare system to screen, early detect and treat patients with cancer.
Type of QI	Outcome
Calculation	a) The 1, 2 and 5-year observed survival rate is computed using the Kaplan Meier survival function.
	b) The 1, 2 and 5-year relative survival is computed as the ratio of:
	• The 1, 2 and 5-year observed survival for the population diagnosed with SCC of the head and neck (= proportion of people surviving 1, 2 and 5 years after the diagnosis)
	and
	• The 1, 2 and 5-year expected observed survival for a comparable group from the general population residing in Belgium (matched on age, gender, region and calendar year [m]).
Target	No target
Data source	• Belgian Cancer Registry (BCR): incidence years 2009-2014
	• Crossroads Bank of Social Security (Kruispuntbank van de Sociale Zekerheid (KSZ) - Banque Carrefour de la Sécurité Sociale (BCSS)) for mortality data (vital status of patients diagnosed with cancer): follow-up until 14 December 2017
	• IMA data for subgroup analyses
Technical definition	Diagnosis of HNSCC: ICD-O-3 (RARECAREnet, layer 2) (Appendix 1)
	Treatments: surgery with curative intent (IMA, Table 38 – Table 47), radiotherapy with curative intent (IMA, Table 48), chemotherapy (IMA, Table 54), targeted therapy (IMA, Table 55), palliative radiotherapy (Table 49)

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[m]   For the relative survival estimation, the survival time is split into 1-year wide intervals. Within these 1-year intervals, the expected survival is obtained from the national lifetables which are stratified on gender, age, region and calendar year. For example, consider a male patient diagnosed at age sixty in 2008 who survived at least three years. In the 2-3 year interval, this patient was 62 in 2010, the corresponding empirical probability in the general male population to die at this age in 2010 is 1.28%.

Title	The 1, 2 and 5-year observed and relative survival after a diagnosis of head & neck SCC

Risk adjustment	For all HNSCC patients:
	    a. by tumour and patient characteristics
	    b. by treatment modality received
	Patient characteristics: gender, age at diagnosis, Adapted Charlson Comorbidity Index , WHO performance status and previous inpatient bed days
	Tumour characteristics: anatomic site (i.e. oral cavity, larynx, oropharynx and hypopharynx), combined stage

Limitations	Volumes are restricted to the selection criteria of the study (e.g. patients with multiple malignancies were excluded). Curative intent cannot be defined from the administrative databases. There are residual confounding factors (e.g. SES background) for which no adjustments can be made.
Subgroup analyses	Cf. risk adjustment
Sensitivity analyses	Median survival time

Benchmarking	Analyses per centre
	    all HNSCC patients, subgroups by tumour localisation (per diagnostic centre and per treatment centre)
	    subgroup of operated patients (by centre where surgery was performed)
	    subgroup of primary radiotherapy (by centre where radiotherapy was performed)
	    subgroup of primary chemotherapy/targeted therapy (by centre where chemotherapy/targeted therapy was performed)
	Patients treated in one centre vs. more than one centre
	Observed survival: Adjusted for case-mix (i.e. age at diagnosis, gender, anatomic site, stage, Adapted Charlson Comorbidity Index, WHO performance status)

Results

Table 138 – 1-, 2-, and 5-year unadjusted observed and relative survival, median survival, by patient and tumour characteristics (2009-2014)

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
Overall	9 245	76.5 (75.7, 77.4)	65.0 (64.0, 66.0)	49.2 (48.2, 50.3)	78.2 (77.4, 79.2)	67.8 (66.8, 68.8)	55.0 (53.9, 56.2)	4.8
Anatomic site								
Oral cavity	2 665	76.3 (74.6, 77.9)	65.1 (63.3, 66.9)	50.1 (48.2, 52.1)	78.1 (76.4, 79.7)	68.0 (66.1, 69.9)	55.8 (53.7, 58.1)	5.1
Oropharynx	2 745	74.2 (72.6, 75.9)	61.4 (59.6, 63.2)	44.7 (42.8, 46.7)	75.5 (73.9, 77.2)	63.5 (61.7, 65.4)	48.9 (46.9, 51.1)	3.7
Hypopharynx	1 137	65.6 (62.8, 68.4)	49.5 (46.6, 52.4)	30.7 (27.9, 33.6)	66.9 (64.0, 69.6)	51.3 (48.3, 54.3)	33.7 (30.7, 36.8)	2.0
Larynx	2 698	83.8 (82.4, 85.2)	74.9 (73.3, 76.6)	60.6 (58.7, 62.5)	86.0 (84.6, 87.5)	78.9 (77.2, 80.7)	69.5 (67.3, 71.7)	8.0
Gender								
Male	7 017	76.0 (75.0, 77.0)	63.8 (62.7, 65.0)	47.6 (46.5, 48.9)	77.7 (76.7, 78.7)	66.6 (65.5, 67.8)	53.5 (52.2, 54.9)	4.3
Female	2 228	78.4 (76.7, 80.1)	68.6 (66.7, 70.5)	54.2 (52.1, 56.3)	80.1 (78.3, 81.8)	71.3 (69.3, 73.3)	59.7 (57.4, 62.1)	6.3
Age at diagnosis (years)								
<50	930	85.5 (83.1, 87.7)	73.4 (70.5, 76.2)	59.9 (56.6, 63.0)	85.7 (83.4, 87.9)	73.8 (70.9, 76.6)	60.7 (57.4, 63.9)	>8.9
50-59	3 058	81.0 (79.6, 82.4)	69.4 (67.8, 71.0)	52.4 (50.6, 54.2)	81.6 (80.2, 83.0)	70.4 (68.7, 72.0)	54.4 (52.5, 56.3)	5.8
60-69	3 047	76.3 (74.8, 77.8)	65.0 (63.4, 66.7)	50.0 (48.2, 51.9)	77.3 (75.8, 78.9)	67.0 (65.2, 68.7)	54.4 (52.4, 56.4)	5.0
70-79	1 481	71.8 (69.5, 74.1)	60.4 (57.9, 62.9)	45.9 (43.3, 48.5)	74.5 (72.1, 76.8)	65.1 (62.4, 67.8)	57.0 (53.8, 60.3)	4.0
80 +	729	57.2 (53.5, 60.7)	44.5 (40.9, 48.2)	25.1 (21.9, 28.6)	64.4 (60.3, 68.4)	56.7 (52.1, 61.3)	49.2 (42.9, 55.9)	1.6

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
WHO performance status								
0 – Asymptomatic	1 469	83.7 (81.8, 85.6)	71.5 (69.2, 73.8)	57.1 (54.4, 59.7)	85.2 (83.3, 87.1)	74.1 (71.7, 76.5)	62.8 (59.9, 65.6)	7.6
1 – Symptomatic but completely ambulatory	5 657	77.5 (76.5, 78.7)	66.1 (64.9, 67.4)	49.1 (47.8, 50.5)	79.2 (78.1, 80.3)	68.9 (67.6, 70.2)	54.8 (53.3, 56.4)	4.8
2 – Symptomatic, <50% in bed during the day	228	42.9 (36.5, 49.3)	28.9 (23.2, 34.9)	16.7 (12.1, 22.2)	44.5 (37.8, 51.1)	30.8 (24.7, 37.2)	19.7 (14.3, 26.0)	0.7
3 – Symptomatic, >50% in bed, but not bedbound	104	22.1 (14.7, 30.5)	13.4 (7.8, 20.7)	8.6 (4.2, 15.0)	22.8 (15.2, 31.6)	14.4 (8.3, 22.3)	10.6 (5.2, 18.5)	0.3
4 – Bedbound	37	16.2 (6.6, 29.6)	10.8 (3.4, 23.0)	4.0 (0.4, 15.7)	16.7 (6.8, 30.7)	11.6 (3.7, 24.7)	4.2 (0.4, 17.0)	0.1
Missing	1 750	76.2 (74.2, 78.2)	64.7 (62.5, 67.0)	50.5 (48.1, 52.9)	78.1 (76.1, 80.2)	67.9 (65.5, 70.2)	57.1 (54.4, 59.9)	5.2
Combined stage								
I	1 794	94.1 (93.0, 95.1)	89.5 (88.0, 90.8)	78.1 (76.1, 80.1)	96.2 (95.1, 97.3)	93.6 (92.1, 95.1)	88.3 (86.0, 90.6)	>8.9
II	1 119	86.2 (84.1, 88.1)	76.4 (73.8, 78.8)	60.4 (57.4, 63.3)	88.4 (86.2, 90.3)	80.1 (77.4, 82.6)	68.3 (64.9, 71.6)	8.0
III	1 257	80.5 (78.2, 82.6)	69.2 (66.7, 71.8)	49.6 (46.7, 52.5)	82.3 (80.0, 84.4)	72.2 (69.5, 74.8)	55.2 (52.0, 58.4)	4.9
IV A/B	3 735	69.2 (67.8, 70.7)	54.0 (52.4, 55.6)	36.4 (34.8, 38.0)	70.6 (69.1, 72.1)	55.9 (54.3, 57.6)	39.9 (38.2, 41.7)	2.4
IVC	345	38.8 (33.7, 43.9)	22.3 (18.1, 26.8)	8.3 (5.5, 11.9)	39.7 (34.4, 44.9)	23.3 (18.9, 28.0)	9.6 (6.5, 13.5)	0.7
X (unknown)	995	69.6 (66.7, 72.4)	58.5 (55.5, 61.6)	46.2 (43.0, 49.3)	71.7 (68.7, 74.6)	61.8 (58.5, 65.0)	52.9 (49.3, 56.5)	3.8

Note: If the survival curve remains above 0.5 for the available follow-up period, the median survival cannot be determined; in the table this is indicated as '>8.9' (or in other words: larger than the maximum follow-up time).
Source: BCR – IMA

Table 139 – 1-, 2-, and 5-year unadjusted observed and median survival, by treatment modality (2009-2014)

Treatment modality	N at risk	Observed survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	
Surgery with curative intent	3 518	85.4 (84.2, 86.6)	76.0 (74.6, 77.5)	60.5 (58.8, 62.2)	8.1
(Syst)/RT < Surgery (< adjuvant treatment)	70	78.5 (67.0, 86.5)	62.8 (50.4, 73.0)	49.0 (36.6, 60.3)	4.7
Primary (Syst)RT (no major surgery)	4 596	79.7 (78.5, 80.9)	65.9 (64.6, 67.3)	48.5 (47.0, 50.0)	4.6
Primary systemic therapy (no major surgery, no RT)	381	33.0 (28.4, 37.8)	17.3 (13.7, 21.3)	7.5 (5.1, 10.6)	0.6
Palliative RT	13	7.6 (0.5, 29.2)	7.6 (0.5, 29.2)	0	0.2
No cancer treatment	667	34.3 (30.8, 38.0)	28.3 (25.0, 31.8)	19.7 (16.8, 23.0)	0.3

Syst: systemic treatment
Source: BCR – IMA

Figure 35 – Observed survival, by Adapted Charlson Comorbidity Index and number of inpatient bed days during the previous year (2009-2014)

Source: BCR – IMA – MZG

Table 140 – 1-, 2-, and 5-year unadjusted observed and relative survival, median survival, by patient and tumour characteristics, in patients with SCC of the oral cavity (2009-2014)

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
Anatomic localisation								
Oral cavity	2 665	76.3 (74.6, 77.9)	65.1 (63.3, 66.9)	50.1 (48.2, 52.1)	78.1 (76.4, 79.7)	68.0 (66.1, 69.9)	55.8 (53.7, 58.1)	5.1
Gender								
Male	1 770	75.8 (73.8, 77.8)	63.5 (61.3, 65.8)	47.6 (45.2, 50.0)	77.4 (75.3, 79.4)	66.1 (63.7, 68.4)	52.6 (50.0, 55.3)	4.4
Female	895	77.1 (74.3, 79.8)	68.3 (65.2, 71.3)	55.3 (51.9, 58.7)	79.5 (76.5, 82.2)	71.9 (68.6, 75.0)	62.4 (58.6, 66.2)	6.5
Age at diagnosis (years)								
<50	339	87.2 (83.2, 90.4)	76.8 (72.0, 81.0)	64.3 (58.9, 69.3)	87.4 (83.4, 90.6)	77.2 (72.4, 81.4)	65.1 (59.6, 70.1)	>8.9
50-59	869	82.3 (79.7, 84.8)	71.6 (68.5, 74.5)	54.8 (51.3, 58.2)	82.9 (80.2, 85.3)	72.6 (69.5, 75.5)	56.9 (53.3, 60.4)	6.8
60-69	772	77.3 (74.2, 80.1)	66.5 (63.1, 69.8)	52.2 (48.5, 55.8)	78.3 (75.2, 81.2)	68.4 (64.9, 71.7)	56.4 (52.4, 60.3)	5.4
70-79	410	68 (63.3, 72.3)	55.1 (50.2, 59.8)	40.7 (35.8, 45.8)	70.3 (65.5, 74.8)	59.0 (53.8, 64.1)	49.8 (43.7, 55.8)	3.1
80 +	275	53 (47.0, 58.8)	41.4 (35.6, 47.2)	25.7 (20.4, 31.3)	59.9 (53.1, 66.4)	52.7 (45.3, 60.0)	48.7 (38.8, 59.3)	1.3
WHO performance status								
0 – Asymptomatic	429	82.4 (78.5, 85.7)	70.7 (66.1, 74.8)	58.1 (53.1, 62.7)	84 (80.1, 87.4)	73.3 (68.6, 77.6)	63.7 (58.3, 68.8)	>8.9
1 – Symptomatic but completely ambulatory	1 519	76.8 (74.7, 78.9)	66.3 (63.9, 68.7)	50.1 (47.5, 52.8)	78.6 (76.4, 80.7)	69.1 (66.6, 71.5)	55.5 (52.6, 58.5)	5.1
2 – Symptomatic, <50% in bed during the day	62	32.2 (21.1, 43.9)	20.9 (11.9, 31.8)	11 (4.8, 20.3)	33.4 (21.9, 45.5)	22.2 (12.6, 33.7)	12.4 (5.2, 23.4)	0.6

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
3 – Symptomatic, >50% in bed, but not bedbound	23	21.7 (7.9, 39.9)	4.3 (0.3, 18.2)	4.3 (0.3, 18.2)	22.9 (8.3, 42.1)	5.0 (0.4, 21.1)	6.3 (0.5, 26.8)	0.2
4 – Bedbound	8	37.5 (8.7, 67.4)	37.5 (8.7, 67.4)	0	39.3 (9.1, 70.8)	39.7 (9.2, 71.5)	0	0.6
Missing	624	77.5 (74.0, 80.6)	65.4 (61.6, 69.1)	50.8 (46.8, 54.8)	79.6 (76.1, 82.8)	68.9 (64.8, 72.7)	57.7 (53.1, 62.2)	5.3
Combined stage								
I	677	93.6 (91.5, 95.2)	88.7 (86.1, 90.9)	78.2 (74.8, 81.3)	95.4 (93.3, 97.1)	92.1 (89.4, 94.4)	86.4 (82.7, 89.9)	>8.9
II	392	83.6 (79.6, 87.0)	75 (70.4, 79.0)	58.3 (53.0, 63.2)	86.0 (81.9, 89.4)	78.7 (74.0, 83.0)	65.9 (60.0, 71.5)	7.2
III	288	78.4 (73.3, 82.8)	65.6 (59.8, 70.8)	47.4 (41.4, 53.3)	80.2 (74.9, 84.7)	68.2 (62.2, 73.6)	51.9 (45.3, 58.3)	4.5
IV A/B	969	64.9 (61.9, 67.9)	49.8 (46.6, 52.9)	32.7 (29.7, 35.8)	66.4 (63.3, 69.4)	51.9 (48.6, 55.1)	36.1 (32.8, 39.6)	2.0
IVC	56	30.3 (19.0, 42.5)	16 (7.9, 26.8)	7.1 (2.3, 15.8)	30.9 (19.4, 43.4)	16.6 (8.2, 27.7)	7.6 (2.5, 17.0)	0.5
X (unknown)	283	70.2 (64.6, 75.2)	56.7 (50.8, 62.3)	42.7 (36.8, 48.5)	72.7 (66.9, 77.9)	60.6 (54.2, 66.5)	49.6 (42.8, 56.4)	2.9
Previous inpatient bed days								
None	533	80.6 (77.0, 83.8)	70.2 (66.2, 74.0)	60.3 (55.9, 64.5)	82.9 (79.2, 86.1)	73.8 (69.6, 77.8)	67.8 (62.8, 72.5)	>8.9
1-5 days	1 298	83 (80.9, 85.0)	73.4 (71.0, 75.8)	57.6 (54.8, 60.4)	84.7 (82.6, 86.7)	76.4 (73.8, 78.8)	63.6 (60.6, 66.7)	7.6
6-15 days	490	70.9 (66.7, 74.7)	56.7 (52.2, 61.0)	39.4 (34.9, 43.8)	72.4 (68.1, 76.3)	59.0 (54.4, 63.5)	43.6 (38.7, 48.6)	2.8
>15 days	344	51.7 (46.3, 56.9)	37.7 (32.7, 42.9)	21.7 (17.4, 26.5)	53.4 (47.9, 58.8)	40.0 (34.6, 45.5)	25.0 (20.1, 30.5)	1.1

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
Adapted Charlson Comorbidity Index								
0	1 548	82.4 (80.4, 84.2)	72 (69.8, 74.3)	57.3 (54.8, 59.9)	84.0 (82.0, 85.9)	74.8 (72.5, 77.1)	63.3 (60.4, 66.1)	7.9
1-2	777	71.9 (68.6, 75.0)	60.6 (57.1, 63.9)	44.5 (40.9, 48.2)	73.7 (70.3, 76.8)	63.4 (59.8, 67.0)	49.9 (45.9, 53.9)	3.4
3-4	145	56.5 (48.1, 64.2)	42.7 (34.6, 50.6)	21.5 (15.0, 28.9)	58.4 (49.7, 66.3)	45.3 (36.8, 53.8)	24.6 (17.2, 33.0)	1.3
>4	35	37.1 (21.6, 52.7)	17.1 (7.0, 31.1)	8.5 (2.2, 20.6)	38.6 (22.5, 54.8)	18.3 (7.4, 33.2)	9.9 (2.5, 23.8)	0.7
Missing	160	65 (57.1, 71.8)	51.2 (43.3, 58.7)	43.7 (35.8, 51.4)	67.9 (59.7, 75.1)	55.2 (46.7, 63.3)	51.0 (41.8, 60.0)	2.2
Treatment modality								
Surgery with curative intent	1 957	84.3 (82.7, 85.9)	74.6 (72.6, 76.5)	59 (56.8, 61.3)	86.1 (84.4, 87.7)	77.6 (75.6, 79.6)	65.5 (63.0, 68.0)	7.6
(Syst)/RT < Surgery (< adjuvant treatment)	15	66.6 (37.5, 84.6)	60 (31.8, 79.7)	52.5 (25.2, 74.0)	68.4 (38.5, 86.8)	62.7 (33.2, 83.3)	58.5 (28.1, 82.4)	>8.4
Primary (Syst)RT (no major surgery)	404	63.1 (58.2, 67.6)	43.3 (38.4, 48.1)	27.3 (23.0, 31.9)	64.7 (59.7, 69.3)	45.2 (40.2, 50.3)	30.5 (25.7, 35.6)	1.6
Primary systemic therapy (no major surgery, no RT)	85	31.7 (22.2, 41.7)	20 (12.3, 29.1)	8.6 (3.8, 16.1)	32.1 (22.5, 42.3)	20.4 (12.6, 29.8)	8.9 (3.8, 16.9)	0.6
Palliative RT	4	0	0	0	0	NA (FU<2yr)	NA (FU<5yr)	0.2
No cancer treatment	200	45 (38.0, 51.7)	38 (31.3, 44.7)	28.3 (22.2, 34.8)	47.4 (40.0, 54.5)	41.4 (34.1, 48.7)	33.3 (26.1, 41.0)	0.6

Note: If the survival curve remains above 0.5 for the available follow-up period, the median survival cannot be determined; in the table this is indicated as '>8.9' (or in other words: larger than the maximum Follow-up time).
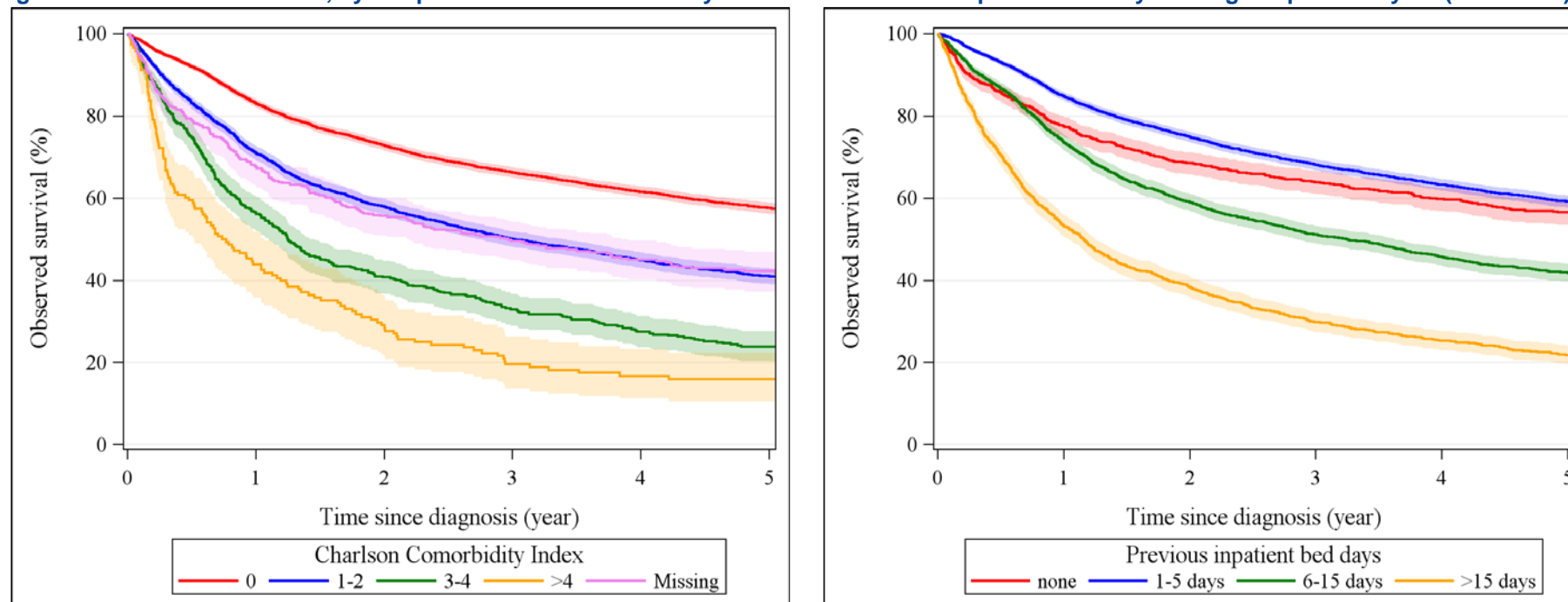*Source: BCR – IMA – MZG*

Table 141 – 1-, 2-, and 5-year unadjusted observed and relative survival, median survival, by patient and tumour characteristics, in patients with oropharyngeal SCC (2009-2014)

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
Anatomic localisation								
Oropharynx	2 745	74.2 (72.6, 75.9)	61.4 (59.6, 63.2)	44.7 (42.8, 46.7)	75.5 (73.9, 77.2)	63.5 (61.7, 65.4)	48.9 (46.9, 51.1)	3.7
Gender								
Male	1 998	72.6 (70.6, 74.5)	58.9 (56.8, 61.1)	42.2 (40.0, 44.5)	73.9 (71.9, 75.9)	61.1 (58.9, 63.3)	46.3 (43.9, 48.8)	3.2
Female	747	78.7 (75.6, 81.5)	68.0 (64.5, 71.2)	51.5 (47.8, 55.2)	79.90 (76.8, 82.8)	70.0 (66.5, 73.4)	55.9 (51.8, 59.9)	5.3
Age at diagnosis (years)								
<50	319	80.8 (76.1, 84.8)	67.7 (62.3, 72.5)	51.0 (45.4, 56.5)	81.1 (76.3, 85.0)	68.1 (62.6, 73.0)	51.9 (46.1, 57.4)	5.5
50-59	1 013	79.2 (76.6, 81.6)	65.7 (62.7, 68.5)	47.9 (44.8, 51.1)	79.7 (77.1, 82.2)	66.6 (63.6, 69.5)	49.7 (46.4, 53.0)	4.3
60-69	916	72.8 (69.8, 75.6)	59.7 (56.5, 62.8)	45.2 (41.8, 48.6)	73.8 (70.8, 76.6)	61.4 (58.1, 64.6)	49.1 (45.4, 52.7)	3.8
70-79	364	64.8 (59.7, 69.5)	54.6 (49.4, 59.6)	38.0 (32.9, 43.3)	67.1 (61.8, 71.9)	58.7 (53.1, 64.0)	46.8 (40.5, 53.3)	2.7
80 +	133	56.3 (47.5, 64.3)	44.3 (35.8, 52.6)	19.1 (12.4, 27.1)	63.7 (53.7, 72.7)	56.7 (45.8, 67.3)	38.4 (25.2, 53.9)	1.4
WHO performance status								
0 – Asymptomatic	463	81.2 (77.3, 84.5)	70.8 (66.5, 74.8)	54.9 (50.2, 59.5)	82.3 (78.5, 85.7)	72.9 (68.5, 77.0)	59.6 (54.5, 64.6)	6.9
1 – Symptomatic but completely ambulatory	1 714	75.9 (73.9, 77.9)	62.4 (60.1, 64.7)	44.8 (42.4, 47.3)	77.2 (75.1, 79.2)	64.4 (62.1, 66.8)	49.0 (46.3, 51.7)	3.8
2 – Symptomatic, <50% in bed during the day	73	50.6 (38.7, 61.4)	32.8 (22.5, 43.7)	15.6 (8.3, 25.1)	51.8 (39.7, 62.9)	34.3 (23.5, 45.6)	17.4 (9.3, 27.8)	1.1

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
3 – Symptomatic, >50% in bed, but not bedbound	29	27.5 (13.1, 44.3)	17.2 (6.3, 32.7)	10.3 (2.6, 24.3)	28.3 (13.4, 45.5)	18.3 (6.7, 34.9)	14.0 (3.6, 33.0)	0.3
4 – Bedbound	17	5.8 (0.4, 23.5)	0	0	5.9 (0.4, 23.9)	0	NA (FU<5yr)	0.1
Missing	449	70.1 (65.7, 74.2)	57.9 (53.2, 62.3)	42.4.0 (37.7, 47.1)	71.6 (67.1, 75.8)	60.2 (55.4, 64.9)	46.8 (41.6, 52.0)	3.0
Combined stage								
I	221	92.3 (87.9, 95.1)	84.6 (79.1, 88.8)	62.1 (54.9, 68.6)	93.8 (89.4, 96.7)	87.4 (81.8, 91.7)	68.1 (60.2, 75.2)	8.3
II	264	87.5 (82.9, 90.9)	76.8 (71.3, 81.5)	61.2 (54.9, 67.1)	88.8 (84.2, 92.4)	79.3 (73.6, 84.1)	66.6 (59.8, 72.9)	8.1
III	409	81.9 (77.8, 85.3)	70.4 (65.7, 74.6)	51.7 (46.7, 56.7)	83.3 (79.2, 86.8)	72.8 (68.0, 77.1)	56.7 (51.1, 62.1)	5.4
IV A/B	1 465	72.1 (69.8, 74.4)	57.8 (55.2, 60.3)	41.4 (38.8, 44.0)	73.4 (71.0, 75.7)	59.7 (57.1, 62.4)	45.2 (42.4, 48.1)	2.9
IVC	139	43.8 (35.5, 51.9)	27.3 (20.2, 34.9)	10.9 (5.8, 17.9)	44.6 (36.2, 52.9)	28.2 (20.9, 36.1)	12.8 (7.3, 20.1)	0.9
X (unknown)	247	61.0 (54.6, 66.8)	50 (43.6, 56.1)	38.0 (31.8, 44.2)	62.4 (55.9, 68.4)	52.1 (45.5, 58.5)	41.9 (35.1, 48.7)	2.0
Previous inpatient bed days								
None	332	73.1 (68.1, 77.6)	64.1 (58.7, 69.1)	49.8 (44.2, 55.3)	74.9 (69.7, 79.5)	66.9 (61.3, 72.1)	54.8 (48.5, 60.9)	4.7
1-5 days	1 276	82.1 (80.0, 84.2)	70.9 (68.4, 73.4)	54.6 (51.8, 57.5)	83.5 (81.3, 85.6)	73.3 (70.7, 75.8)	59.7 (56.6, 62.8)	7.2
6-15 days	712	73.3 (69.9, 76.4)	57.3 (53.6, 60.8)	39.3 (35.6, 43.1)	74.3 (70.9, 77.5)	58.9 (55.1, 62.6)	42.6 (38.6, 46.6)	2.9
>15 days	425	52.9 (48.1, 57.6)	37.6 (33.0, 42.2)	20.4 (16.6, 24.5)	54.1 (49.2, 58.9)	39.3 (34.5, 44.1)	22.9 (18.7, 27.6)	1.1

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
Adapted Charlson Comorbidity Index								
0	1 598	81.4 (79.4, 83.2)	69.7 (67.4, 71.9)	53.2 (50.7, 55.8)	82.6 (80.6, 84.5)	71.9 (69.5, 74.2)	57.9 (55.1, 60.7)	6.2
1-2	769	66.0 (62.6, 69.3)	52.0 (48.4, 55.5)	34.4 (31.0, 38.0)	67.2 (63.7, 70.6)	53.8 (50.1, 57.5)	38.0 (34.2, 41.8)	2.3
3-4	183	57.3 (49.9, 64.2)	40.9 (33.8, 48.0)	26.9 (20.6, 33.7)	58.6 (50.9, 65.5)	42.6 (35.2, 49.9)	29.7 (22.8, 37.2)	1.3
>4	43	55.8 (39.8, 69.1)	34.8 (21.2, 48.9)	17.7 (7.9, 30.7)	57.1 (40.8, 70.7)	36.5 (22.2, 51.2)	19.3 (8.5, 33.8)	1.1
Missing	152	66.4 (58.3, 73.3)	53.9 (45.7, 61.5)	35.6 (27.6, 43.9)	68.6 (60.3, 75.8)	57.1 (48.4, 65.2)	40.5 (31.2, 50.0)	2.6
Treatment modality								
Surgery with curative intent	644	85.8 (82.9, 88.3)	78.2 (74.9, 81.3)	60.7 (56.7, 64.6)	87.0 (84.1, 89.6)	80.5 (77.0, 83.6)	65.8 (61.5, 70.0)	8.3
(Syst)/RT < Surgery (< adjuvant treatment)	27	77.7 (57.1, 89.3)	59.2 (38.6, 75.0)	48.1 (28.7, 65.2)	78.7 (57.8, 90.5)	60.8 (39.7, 77.0)	51.2 (30.2, 69.7)	3.1
Primary (Syst)RT (no major surgery)	1 724	79.5 (77.5, 81.3)	64.2 (61.9, 66.5)	46.1 (43.6, 48.5)	80.8 (78.8, 82.7)	66.4 (64.0, 68.7)	50.5 (47.8, 53.2)	4.1
Primary systemic therapy (no major surgery, no RT)	144	34.7 (27.1, 42.5)	19.4 (13.4, 26.3)	9.6 (5.5, 15.1)	35.2 (27.5, 43.1)	20.0 (13.8, 27.0)	10.3 (5.9, 16.3)	0.6
Palliative RT	3	33.3 (0.9, 77.4)	33.3 (0.9, 77.4)	0	33.7 (0.9, 78.3)	33.8 (0.9, 78.6)	NA (FU<5yr)	0.4
No cancer treatment	203	21.1 (15.9, 27.0)	14.7 (10.3, 20.0)	7.2 (4.0, 11.7)	22.0 (16.5, 28.1)	16.0 (11.2, 21.7)	8.5 (4.7, 14.0)	0.2

Note: If the survival curve remains above 0.5 for the available follow-up period, the median survival cannot be determined; in the table this is indicated as '>8.9' (or in other words: larger than the maximum Follow-up time).
Source: BCR – IMA – MZG

Table 142 – 1-, 2-, and 5-year unadjusted observed and relative survival, median survival, by patient and tumour characteristics, in patients with hypopharyngeal SCC (2009-2014)

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
Anatomic localisation								
Hypopharynx	1 137	65.6 (62.8, 68.4)	49.5 (46.6, 52.4)	30.7 (27.9, 33.6)	66.9 (64.0, 69.6)	51.3 (48.3, 54.3)	33.7 (30.7, 36.8)	2.0
Gender								
Male	974	65.9 (62.8, 68.8)	49.9 (46.8, 53.1)	31.0 (28.0, 34.2)	67.1 (64.1, 70.1)	51.8 (48.5, 55.0)	34.2 (30.9, 37.6)	2.0
Female	163	64.2 (56.4, 71.1)	46.9 (39.1, 54.4)	28.6 (21.7, 36.0)	65.2 (57.3, 72.2)	48.3 (40.3, 56.0)	30.8 (23.3, 38.7)	1.8
Age at diagnosis (years)								
<50	84	82.0 (72.0, 88.7)	57.8 (46.6, 67.7)	40.6 (30.0, 51.0)	82.2 (72.2, 89.0)	58.2 (46.9, 68.1)	41.3 (30.4, 51.9)	2.4
50-59	437	72.7 (68.3, 76.7)	56.5 (51.7, 61.0)	34.4 (29.8, 39.1)	73.2 (68.8, 77.2)	57.3 (52.5, 61.9)	35.9 (31.2, 40.8)	2.6
60-69	411	62.5 (57.7, 67.0)	46.9 (42.1, 51.7)	29.7 (25.0, 34.5)	63.4 (58.5, 68.0)	48.4 (43.4, 53.3)	32.5 (27.5, 37.8)	1.8
70-79	146	56.1 (47.7, 63.8)	41.7 (33.7, 49.6)	24.1 (17.1, 31.8)	58.0 (49.4, 66.0)	44.7 (36.2, 53.2)	29.8 (21.3, 39.2)	1.5
80 +	59	35.5 (23.7, 47.7)	23.7 (13.8, 35.1)	11.4 (4.9, 21.1)	40.0 (26.6, 53.6)	30.1 (17.6, 44.6)	22.8 (9.8, 41.9)	0.5
WHO performance status								
0 – Asymptomatic	175	75.4 (68.3, 81.1)	53.1 (45.5, 60.2)	35.8 (28.6, 43.2)	76.5 (69.4, 82.4)	54.7 (46.9, 62.1)	38.9 (31.1, 46.9)	2.3
1 – Symptomatic but completely ambulatory	756	66.7 (63.3, 70.0)	51.9 (48.3, 55.4)	30.6 (27.2, 34.2)	67.9 (64.5, 71.3)	53.7 (50.0, 57.4)	33.8 (30.1, 37.7)	2.1
2 – Symptomatic, <50% in bed during the day	35	31.4 (17.1, 46.8)	28.5 (14.9, 43.8)	22.2 (10.2, 37.2)	32.5 (17.7, 48.5)	30.1 (15.7, 46.3)	24.8 (11.3, 41.6)	0.3

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
3 – Symptomatic, >50% in bed, but not bedbound	14	21.4 (5.2, 44.8)	14.2 (2.3, 36.6)	NA (FU<5yr)	22.1 (5.4, 46.4)	15.0 (2.4, 38.4)	NA (FU<5yr)	0.2
4 – Bedbound	6	0	0	0	0	NA (FU<2yr)	NA (FU<5yr)	0.1
Missing	151	63.5 (55.4, 70.7)	43.7 (35.7, 51.4)	30.1 (22.8, 37.7)	64.7 (56.4, 72.0)	45.1 (36.9, 53.1)	32.7 (24.8, 41.1)	1.5
Combined stage								
I	43	90.6 (77.1, 96.4)	76.7 (61.1, 86.7)	57.8 (41.7, 71.0)	92.7 (78.8, 98.6)	80.2 (63.9, 90.7)	65.2 (46.8, 80.4)	5.6
II	74	75.6 (64.2, 83.9)	60.8 (48.7, 70.9)	38.3 (26.9, 49.7)	77.1 (65.4, 85.5)	62.9 (50.5, 73.4)	41.9 (29.6, 54.2)	3.6
III	174	77.5 (70.6, 83.1)	67.2 (59.7, 73.7)	45.9 (38.0, 53.5)	79.1 (72.1, 84.8)	69.8 (62.1, 76.6)	50.9 (42.2, 59.3)	4.2
IVA/B	661	66.8 (63.1, 70.3)	48.3 (44.5, 52.1)	28.8 (25.3, 32.6)	67.9 (64.2, 71.5)	49.8 (45.9, 53.8)	31.4 (27.6, 35.4)	1.9
IVC	89	31.4 (22.1, 41.2)	17.9 (10.8, 26.6)	2.3 (0.3, 9.2)	32.1 (22.6, 42.1)	18.7 (11.3, 27.7)	3.3 (0.7, 10.0)	0.7
X (unknown)	96	48.9 (38.6, 58.5)	34.3 (25.1, 43.9)	23.7 (15.5, 33.0)	50.1 (39.6, 59.9)	35.7 (26.1, 45.6)	26.4 (17.4, 36.7)	0.9
Previous inpatient bed days								
None	60	50.0 (36.8, 61.8)	40.0 (27.7, 52.0)	27.5 (16.7, 39.4)	51.7 (38.1, 63.9)	42.4 (29.3, 55.2)	31.2 (18.9, 44.9)	1.0
1-5 days	486	75.7 (71.7, 79.3)	60.6 (56.2, 64.9)	38.8 (34.3, 43.4)	77.0 (72.9, 80.6)	62.6 (58.1, 67.0)	42.6 (37.6, 47.6)	2.9
6-15 days	338	65.6 (60.4, 70.5)	46.7 (41.3, 52.0)	30.0 (24.9, 35.2)	66.8 (61.4, 71.7)	48.2 (42.7, 53.7)	32.6 (27.2, 38.3)	1.8
>15 days	253	50.1 (43.8, 56.1)	34.1 (28.4, 40.1)	17.1 (12.6, 22.2)	51.1 (44.7, 57.2)	35.4 (29.4, 41.5)	18.8 (13.9, 24.5)	1.1
Adapted Charlson Comorbidity Index								

		Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
Characteristics	N at risk	1-year	2-year	5-year	1-year	2-year	5-year	
0	609	72.4 (68.7, 75.8)	57.6 (53.6, 61.4)	36.3 (32.4, 40.4)	73.5 (69.8, 77.0)	59.3 (55.2, 63.3)	39.4 (35.1, 43.7)	2.6
1-2	393	61.0 (56.0, 65.6)	42.6 (37.7, 47.5)	25.9 (21.5, 30.6)	62.3 (57.2, 67.0)	44.4 (39.3, 49.5)	29.1 (24.2, 34.4)	1.6
3-4	69	53.6 (41.2, 64.5)	34.7 (23.8, 45.9)	18.6 (10.1, 29.1)	54.5 (42.0, 65.7)	35.9 (24.6, 47.4)	20.1 (11.0, 31.4)	1.2
>4	28	35.7 (18.9, 53.0)	25 (11.1, 41.8)	17.8 (6.5, 33.7)	36.2 (19.1, 53.8)	25.7 (11.4, 43.0)	19.0 (7.0, 36.0)	0.5
Missing	38	50.0 (33.4, 64.5)	36.8 (22.0, 51.8)	22.5 (10.6, 37.3)	51.6 (34.5, 66.6)	39.0 (23.3, 54.9)	24.8 (11.5, 41.5)	1.0
Treatment modality								
Surgery with curative intent	154	82.4 (75.5, 87.6)	63.6 (55.5, 70.7)	43.8 (35.4, 52.1)	83.6 (76.6, 88.9)	65.4 (57.1, 72.7)	47.9 (38.8, 56.6)	4.0
(Syst)/RT < Surgery (< adjuvant treatment)	6	50.0 (11.1, 80.4)	50.0 (11.1, 80.4)	NA (FU<5yr)	50.7 (11.3, 81.5)	51.3 (11.4, 82.6)	NA (FU<5yr)	1.7
Primary (Syst)RT (no major surgery)	795	72.8 (69.6, 75.8)	55.8 (52.3, 59.2)	34.8 (31.4, 38.3)	74.0 (70.8, 77.1)	57.6 (54.0, 61.2)	38.2 (34.4, 42.0)	2.5
Primary systemic therapy (no major surgery, no RT)	94	27.6 (19.1, 36.9)	10.6 (5.4, 17.8)	2.1 (0.4, 6.7)	28.1 (19.4, 37.6)	11.0 (5.7, 18.5)	2.2 (0.4, 7.3)	0.6
Palliative RT	2	0	0	0	0	NA (FU<2yr)	NA (FU<5yr)	0.3
No cancer treatment	86	13.9 (7.6, 22.1)	10.4 (5.1, 18.0)	3.4 (0.9, 9.0)	14.5 (8.0, 23.0)	11.1 (5.5, 19.1)	3.6 (0.9, 9.8)	0.2

Note: If the survival curve remains above 0.5 for the available follow-up period, the median survival cannot be determined; in the table this is indicated as '>8.9' (or in other words: larger than the maximum Follow-up time); FU: follow-up; NA: not applicable
Source: BCR – IMA – MZG

Table 143 – 1-, 2-, and 5-year unadjusted observed and relative survival, median survival, by patient and tumour characteristics, in patients with laryngeal SCC (2009-2014)

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
Anatomic localisation								
Larynx	2 698	83.8 (82.4, 85.2)	74.9 (73.3, 76.6)	60.6 (58.7, 62.5)	86.0 (84.6, 87.5)	78.9 (77.2, 80.7)	69.5 (67.3, 71.7)	8.0
Gender								
Male	2 275	83.4 (81.9, 84.9)	74.2 (72.4, 76.0)	59.5 (57.4, 61.6)	85.8 (84.2, 87.3)	78.5 (76.6, 80.4)	69.0 (66.6, 71.4)	7.6
Female	423	86.0 (82.4, 89.0)	78.7 (74.5, 82.3)	66.4 (61.6, 70.8)	87.5 (83.8, 90.5)	81.3 (77.0, 85.1)	72.3 (67.1, 77.2)	>8.8
Age at diagnosis (years)								
<50	188	91.9 (87.1, 95.1)	83.9 (77.9, 88.5)	75.3 (68.4, 81.0)	92.2 (87.3, 95.4)	84.4 (78.3, 89.0)	76.5 (69.4, 82.3)	>8.9
50-59	739	86.9 (84.3, 89.2)	79.6 (76.6, 82.4)	66.3 (62.7, 69.7)	87.5 (84.9, 89.8)	80.8 (77.7, 83.6)	69.0 (65.2, 72.6)	>8.9
60-69	948	84.8 (82.4, 86.9)	76.8 (74.1, 79.5)	61.6 (58.3, 64.8)	86.0 (83.6, 88.2)	79.2 (76.4, 81.9)	67.1 (63.6, 70.6)	8
70-79	561	83.3 (80.0, 86.2)	73.0 (69.2, 76.5)	60.1 (55.9, 64.2)	86.6 (83.2, 89.6)	79.1 (74.9, 82.9)	75.9 (70.5, 80.9)	6.7
80 +	262	66.7 (60.7, 72.1)	52.6 (46.5, 58.5)	30.4 (24.6, 36.5)	75.0 (68.3, 81.1)	66.9 (59.1, 74.4)	60.7 (49.2, 72.6)	2.4
WHO performance status								
0 – Asymptomatic	402	91.7 (88.6, 94.1)	81.3 (77.2, 84.8)	67.6 (62.7, 72.2)	93.7 (90.5, 96.1)	84.9 (80.6, 88.6)	75.9 (70.3, 81.1)	>8.9
1 – Symptomatic but completely ambulatory	1 668	84.8 (83.0, 86.4)	76.2 (74.1, 78.2)	60.8 (58.3, 63.2)	87.0 (85.2, 88.7)	80.2 (78.1, 82.4)	69.8 (67.0, 72.6)	7.6
2 – Symptomatic, <50% in bed during the day	58	51.7 (38.2, 63.6)	32.7 (21.2, 44.8)	21.4 (11.2, 33.9)	54.5 (40.3, 67.1)	35.9 (23.2, 49.1)	28.8 (15.7, 44.5)	1.1

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
3 – Symptomatic, >50% in bed, but not bedbound	38	18.4 (8.1, 32.0)	15.7 (6.4, 28.9)	10.5 (3.3, 22.5)	18.9 (8.3, 32.9)	16.4 (6.7, 30.2)	11.4 (3.7, 24.6)	0.3
4 – Bedbound	6	33.3 (4.6, 67.6)	16.6 (0.8, 51.7)	16.6 (0.8, 51.7)	35.0 (4.8, 71.0)	18.9 (0.9, 58.6)	19.7 (0.9, 61.2)	0.4
Missing	526	83.6 (80.2, 86.5)	75.8 (71.9, 79.2)	62.8 (58.4, 66.9)	85.8 (82.4, 88.9)	79.9 (75.9, 83.6)	72.4 (67.5, 77.2)	>8.9
Combined stage								
I	853	95.1 (93.5, 96.4)	92.0 (90.0, 93.7)	83.3 (80.5, 85.8)	97.8 (96.1, 99.1)	97.2 (95.1, 98.9)	96.4 (93.2, 99.4)	>8.9
II	389	89.9 (86.5, 92.6)	80.4 (76.2, 84.1)	66.2 (61.1, 70.9)	92.6 (89.1, 95.4)	85.2 (80.7, 89.1)	77.1 (71.2, 82.5)	8.2
III	386	81.8 (77.6, 85.4)	71.7 (67.0, 76.0)	50.4 (45.1, 55.6)	84.1 (79.8, 87.8)	75.7 (70.7, 80.2)	57.9 (51.7, 63.8)	5.1
IVA/B	640	71.7 (68.1, 75.1)	57.4 (53.5, 61.2)	38.1 (34.3, 42.0)	73.2 (69.5, 76.6)	59.6 (55.6, 63.6)	42.0 (37.8, 46.3)	2.7
IVC	61	45.9 (33.1, 57.8)	22.9 (13.4, 34.1)	9.8 (4.0, 18.8)	47.5 (34.3, 59.8)	24.7 (14.4, 36.7)	12.0 (4.9, 23.0)	0.9
X (unknown)	369	80.4 (76.0, 84.1)	72.0 (67.1, 76.3)	60.1 (54.8, 65.0)	82.7 (78.2, 86.6)	76.1 (71.0, 80.7)	69.6 (63.5, 75.2)	8.4
Previous inpatient bed days								
None	222	83.7 (78.2, 88.0)	78.8 (72.8, 83.6)	65.1 (58.1, 71.3)	86.6 (80.9, 91.0)	84 (77.7, 89.2)	76.6 (68.4, 83.9)	>8.9
1-5 days	1 539	91.4 (90.0, 92.8)	83.9 (82.0, 85.7)	70.6 (68.2, 73.0)	93.7 (92.2, 95.1)	88.2 (86.2, 90.1)	80.9 (78.1, 83.6)	>8.9
6-15 days	542	81.7 (78.2, 84.7)	71.3 (67.3, 75.0)	54.6 (50.3, 58.8)	83.6 (80.0, 86.7)	74.7 (70.5, 78.5)	61.7 (56.8, 66.4)	6.2
>15 days	395	57.0 (52.0, 61.8)	42.8 (37.9, 47.6)	26.6 (22.2, 31.3)	58.9 (53.7, 63.8)	45.5 (40.3, 50.7)	31.4 (26.2, 36.9)	1.3

Characteristics	N at risk	Observed survival (%, 95% CI)			Relative survival (%, 95% CI)			Median observed survival (years)
		1-year	2-year	5-year	1-year	2-year	5-year	
Adapted Charlson Comorbidity Index								
0	1 604	89.6 (88.0, 91.0)	82.5 (80.6, 84.4)	70.0 (67.7, 72.4)	91.8 (90.2, 93.3)	86.7 (84.7, 88.6)	80.0 (77.3, 82.7)	>8.9
1-2	808	80.0 (77.1, 82.6)	68.4 (65.2, 71.6)	51.2 (47.6, 54.7)	82.2 (79.2, 84.9)	72.2 (68.7, 75.5)	58.8 (54.7, 62.9)	5.3
3-4	160	56.2 (48.2, 63.5)	41.2 (33.6, 48.7)	25.1 (18.6, 32.3)	58.4 (50.1, 66.0)	44.6 (36.4, 52.8)	31.0 (22.9, 39.8)	1.3
>4	43	42.8 (27.8, 57.1)	35.7 (21.7, 49.9)	19.0 (8.9, 32.0)	45.2 (29.6, 59.9)	38.7 (23.7, 53.9)	21.7 (10.1, 36.8)	0.7
Missing	83	83.1 (73.2, 89.6)	75.9 (65.2, 83.7)	58.9 (46.8, 69.2)	85.0 (74.9, 91.8)	79.3 (68.1, 87.5)	66.6 (53.3, 77.9)	8.2
Treatment modality								
Surgery with curative intent	763	88.3 (85.8, 90.4)	80.5 (77.6, 83.2)	67.3 (63.7, 70.6)	90.4 (87.9, 92.6)	84.4 (81.3, 87.3)	76.3 (72.3, 80.1)	>8.9
(Syst)/RT < Surgery (< adjuvant treatment)	22	95.4 (71.9, 99.3)	72.7 (49.1, 86.7)	56.9 (33.0, 75.2)	97.9 (73.7, 101.9)	76.7 (51.8, 91.5)	66.3 (38.9, 87.2)	>8.5
Primary (Syst)RT (no major surgery)	1 673	87.2 (85.6, 88.8)	78.1 (76.1, 80.0)	62.4 (60.0, 64.8)	89.4 (87.7, 91.0)	82.1 (80.0, 84.2)	71.6 (68.8, 74.4)	8.2
Primary systemic therapy (no major surgery, no RT)	58	39.6 (27.2, 51.9)	18.9 (10.1, 29.9)	11.0 (4.5, 21.1)	40.3 (27.6, 52.8)	19.5 (10.5, 30.9)	11.9 (4.8, 22.7)	0.6
Palliative RT	4	0	0	0	0	NA (FU<2yr)	NA (FU<5yr)	0.2
No cancer treatment	178	47.4 (40.0, 54.6)	41.8 (34.5, 48.9)	32.2 (25.3, 39.4)	50.1 (42.3, 57.7)	46.1 (38.1, 54.0)	40.7 (32.0, 49.6)	0.8

*Note: If the survival curve remains above 0.5 for the available follow-up period, the median survival cannot be determined; in the table this is indicated as '>8.9' (or in other words: larger than the maximum Foll*ow-up time); FU: follow-up; NA: not applicable

Source: BCR – IMA – MZG

International comparison

Table 144 – Observed and relative survival in HNSCC patients - International results

Author	Period covered	Country	Results
De Ridder et al., 2017[114]	2008	The Netherlands	The **observed** 5-year **survival** for patients with oral cavity SCC (N=602) was 60%; higher age, male gender and higher stage were negatively associated** with overall survival. The 5-year overall survival for patients with oropharyngeal SCC (N=453) was 52%; stage IV and higher age were associated** with a lower overall survival. The 5-year overall survival of laryngeal SCC (N=585) equalled 66%; higher stage, increasing age and female gender were negatively associated** with overall survival. Five-year overall survival for hypopharyngeal SCC (N=175) was 39% with the worst survival (32%) for stage IV patients (due to the low number of events, multivariate analysis could not be performed).
Health and Social Care Information Centre, Tenth Annual Report, 2015[87]	November 2013 - October 2014	England and Wales	For the cohort diagnosed in 2009-2010, the 4-year **crude survival** was 60.7% (95% CI: 58.3 - 63.0) for the 1 652 patients with larynx cancer*, 60.5% (95% CI: 58.3 - 62.6) for the 1 920 patients with oropharynx cancer*, 56.6% (95% CI: 54.3 - 58.8) for the 1 895 patients with oral cavity cancer* and 33.3% (95% CI: 28.8 - 38.2) for the 387 patients with hypopharynx cancer*.
Braakhuis et al., 2014[115]	2007-2011	The Netherlands	The 2- and 5-year **relative survival** for all HNSCC patients (N=10 771) diagnosed between 2007 and 2011 was 72% (95% CI: 72 - 72) and 58% (95% CI: 57 - 60), respectively. The 5-year relative survival rates for the different anatomic sites were: 62% (95% CI: 60 - 64) for oral cavity SCC (N=3 692), 48% (95% CI: 45 - 50) for oropharyngeal SCC (N=2 595), 33% (95% CI: 29 - 37) for hypopharyngeal SCC (N=988), and 70% (95% CI: 68 - 72) for laryngeal SCC (N=3 496).
Guntinas-Lichius et al., 2014[111]	1996-2011	Thuringia[n] (Germany)	The 5- and 10-year **observed survival** (OS) for all patients with head and neck cancer* (N=6 291)*** was 49.1% and 34.1%, respectively. The 5-year OS was lowest for hypopharyngeal cancer* (N=698, 31.6%) and highest for laryngeal cancer* (N=1 388, 58.6%); the 5-year OS for oral cavity* (N=1 642) and oropharyngeal cancer* (N=1 614) equalled 47.5% and 46.9%, respectively.

*Not confined to squamous cell carcinomas; ** Based on a multivariable Cox regression analysis; *** The result for all head and neck cancer cases also includes cancer in the lip, nasopharynx, etc.*

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[n] The federal state Thuringia in the eastern part of Germany had 2 491 119 inhabitants in 1996.(https://statistik.thueringen.de/datenbank/)

Table 145 – 1-, 2- and 5-year observed and relative survival – Comparison between Belgium and other European countries

Anatomic site	Belgium (N=9 245) (2009-2014)	Scotland (N=3 084) (2010-2012)[138]	The Netherlands (N=2 094) (2008)[114]	Thuringia - Germany (N=6 291) (1996-2011) [111]	Belgium (N=9 245) (2009-2014)	The Netherlands (N=10 771) (2007 – 2011)[115]
1-year	Observed survival (%, 95% CI)				Relative survival (%, 95% CI)	
All	76.5 (75.7, 77.4)				78.2 (77.4, 79.2)	
Oral Cavity	76.3 (74.6, 77.9)	77.7*			78.1 (76.4, 79.7)	
Oropharynx	74.2 (72.6, 75.9)	75.4*			75.5 (73.9, 77.2)	
Hypopharynx	65.6 (62.8, 68.4)	55.1*			66.9 (64.0, 69.6)	
Larynx	83.8 (82.4, 85.2)	82.2*			86.0 (84.6, 87.5)	
2-year	Observed survival (%, 95% CI)				Relative survival (%, 95% CI)	
All	65.0 (64.0, 66.0)				67.8 (66.8, 68.8)	72 (72, 72)
Oral Cavity	65.1 (63.3, 66.9)				68.0 (66.1, 69.9)	72 (71, 74)
Oropharynx	61.4 (59.6, 63.2)				63.5 (61.7, 65.4)	64 (62, 66)
Hypopharynx	49.5 (46.6, 52.4)				51.3 (48.3, 54.3)	51 (48, 54)
Larynx	74.9 (73.3, 76.6)				78.9 (77.2, 80.7)	83 (81, 84)
5-year	Observed survival (%, 95% CI)				Relative survival (%, 95% CI)	
All	49.2 (48.2, 50.3)			49.1**	55.0 (53.9, 56.2)	58 (57, 60)
Oral Cavity	50.1 (48.2, 52.1)	52.7*	60	47.5*	55.8 (53.7, 58.1)	62 (60, 64)
Oropharynx	44.7 (42.8, 46.7)	53.1*	52	46.9*	48.9 (46.9, 51.1)	48 (45, 50)
Hypopharynx	30.7 (27.9, 33.6)	16.6*	39	31.6*	33.7 (30.7, 36.8)	33 (29, 37)
Larynx	60.6 (58.7, 62.5)	54.3*	66	58.6*	69.5 (67.3, 71.7)	70 (68, 72)

*Not confined to squamous cell carcinomas; ** The result for all head and neck cancer cases also includes cancer in the lip, nasopharynx, etc.*
Source: BCR – IMA

Appendix 7.5. Association between hospital volume and outcome (V-1)

Appendix 7.5.1. Treatment volume

Documentation sheet

Title	Association between volume of patients with HNSCC and outcome
Rationale	In previous KCE reports the relation between volume of Belgian hospitals and outcomes was evaluated for several cancer types.[2-6] Some of these insights were used to write a report on the organisation of care for adults with rare or complex cancers.[14] The latter report illustrated the ideal organisation of care for fourteen rare or complex cancers around reference centres. According to RARECARE layer 2, that is used for clinical decisions, all HNSCC are considered as rare cancers. Therefore, it was recommended that patients with head and neck cancers should only be treated in a reference centre. Above highly-skilled multidisciplinary teams and adequate facilities to provide high-quality, continuous, and comprehensive care to patients with these types of cancer, a sufficient volume is required to maintain a high level of expertise. An analysis between volume of HNSCC patients treated by centre and patients' overall survival could be helpful to recommend a minimum caseload for reference centres.
Type of QI	Structure
Calculation	Statistical modelling to assess the relation between volume and outcomes (survival and post-treatment mortality), adjusted for potential confounders (see also section 5.5.2)
Target	No target set
Data sources	- Belgian Cancer Registry (BCR): incidence years 2009 – 2014 - Crossroads Bank of Social Security (Kruispuntbank van de Sociale Zekerheid (KSZ) - Banque Carrefour de la Sécurité Sociale (BCSS)) for mortality data (vital status of patients diagnosed with cancer): follow-up until 14 December 2017 - IMA data for subgroup analyses and the definition of confounders
Technical definitions	Three analyses are performed, both using the main treatment centre algorithm (see section 3.3.3): 1. Pooled (for all anatomic sites and all cancer stages together) 2. By anatomic site 3. By combined stage All potential confounders identified beforehand are included in the statistical model: gender, age group, anatomic site, combined stage, WHO performance status, number of previous inpatient bed days and Adapted Charlson Comorbidity Index Outcomes: - 1-, 2- and 5-year overall survival - 30-day all-cause mortality Diagnosis of SCC of the head and neck: RARECAREnet, layer 2 (Appendix 1) Treatments: surgery with curative intent (IMA, Table 38 – Table 47), radiotherapy with curative intent (IMA, Table 48), chemotherapy (IMA, Table 54), targeted therapy (IMA, Table 55)
Risk adjustment	Proportional hazard models for observed survival; logistic regression models for 30-day mortality
Limitations	See discussion section
Subgroup analyses	See technical definitions

Title	Association between volume of patients with HNSCC and outcome
Benchmarking	Main treatment centre
Sensitivity analyses	Association with surgery or radiotherapy (RT) as principal treatment (for overall survival and 30-day mortality)

Technical details

Non-proportional hazards between the levels of categorical covariates were evaluated in a univariate way. Detected non-proportional hazards were resolved with a 'piece-wise proportional hazards model' (i.e. proportionality assumption holds within consecutive time intervals). This implies that the follow-up time is split into subintervals, in each interval proportional hazards are assumed. So in each subinterval there is a HR estimated that is assumed to be constant over that interval. Then all main terms were combined in the Cox model, including their non-proportional hazards. Non-proportional hazards terms that became no longer significant (at the 0.05 significance level) were dropped.

Second order interactions between the main terms were evaluated in a backwards elimination model building procedure. The model assumptions were evaluated on the basis of Schoenfeld and generalised Cox-Snell residuals.

Table 146 – Number and proportion of missing data for confounders (2009-2014)

	All HNSCC (N=9 175)		Main treatment centre ≤ 120 patients in 2009-2014 (N=2 135)		Main treatment centre > 120 patients in 2009-2014 (N=7 040)	
	N	**%**	**N**	**%**	**N**	**%**
Gender	0	0.0	0	0	0	0
Age at diagnosis	0	0.0	0	0	0	0
WHO performance status	1 704	18.6	530	24.8	1 174	16.7
Clinical stage	1 757	19.1	653	30.6	1 104	15.7
Pathological stage						
Patients who had surgery	3 518		1 400		2 118	
X (missing)	760	21.6	376	26.9	384	18.1
Combined stage	957	10.4	306	14.3	651	9.2
Adapted Charlson Comorbidity Index	392	4.3	106	5.0	286	4.1
Number of previous inpatient bed days	0	0	0	0	0	0

Note: Seventy patients are not reported in the table because they could not be assigned to a main treatment centre.
Source: BCR – IMA – MZG

Results - Association between hospital volume and observed survival

INSTITUTIONAL EXPERIENCE: ANALYSIS BY MAIN TREATMENT CENTRE – ALL HNSCC PATIENTS

Table 147 – Estimated HRs for all-cause death, all HNSCC patients, all HNSCC volume, by anatomic site (2009-2014)

Characteristic	HR	95% CI	p-value
Treatment volume, Oral cavity, ≤120	0.999	(0.997, 1.001)	0.3475
Treatment volume, Oral cavity, >120	1.000	(1.000, 1.001)	0.1951
Treatment volume, Oropharynx, ≤120	0.993	(0.991, 0.995)	<0.0001
Treatment volume, Oropharynx, >120	1.000	(0.999, 1.001)	0.8657
Treatment volume, Hypopharynx, ≤120	0.994	(0.991, 0.997)	0.0001
Treatment volume, Hypopharynx, >120	1.000	(0.999, 1.001)	0.9449
Treatment volume, Larynx, ≤120	0.993	(0.991, 0.996)	<0.0001
Treatment volume, Larynx, >120	1.000	(0.999, 1.001)	0.8934

Source: BCR – IMA

Table 148 – Estimated HRs for all-cause death, all HNSCC patients, all HNSCC volume, by combined stage (2009-2014)

Characteristic	HR	95% CI	p-value
Treatment volume, stage I, ≤120	0.999	(0.995, 1.002)	0.5486
Treatment volume, stage I, >120	0.999	(0.999, 1.000)	0.1664
Treatment volume, stage II, ≤120	1.000	(0.996, 1.003)	0.8183
Treatment volume, stage II, >120	1.000	(0.999, 1.001)	0.9377
Treatment volume, stage III, ≤120	0.999	(0.996, 1.003)	0.7972
Treatment volume, stage III, >120	1.000	(0.999, 1.001)	0.9477
Treatment volume, stage IVA-B, ≤120	1.000	(0.996, 1.004)	0.8761
Treatment volume, stage IVA-B, >120	1.000	(1.000, 1.001)	0.4897
Treatment volume, stage IVC, ≤120	0.999	(0.995, 1.003)	0.7405
Treatment volume, stage IVC, >120	1.000	(0.999, 1.001)	0.7113
Treatment volume, stage X, ≤120	1.000	(0.996, 1.004)	0.8686
Treatment volume, stage X, >120	1.001	(1.000, 1.002)	0.0328

Source: BCR – IMA

Figure 36 – Observed survival by main treatment volume over six years in patients with HNSCC (2009-2014)

Stages I and II
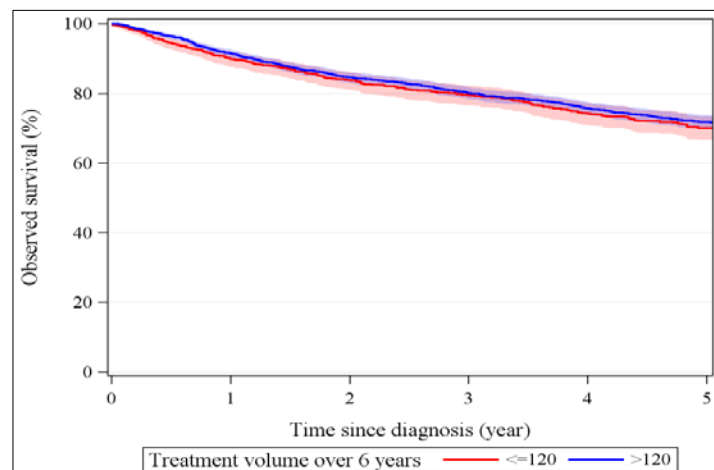
Stages III and IVA-B
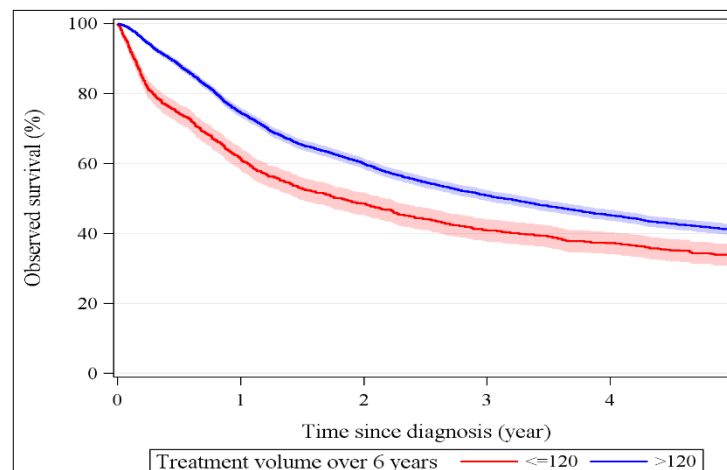
Stage X
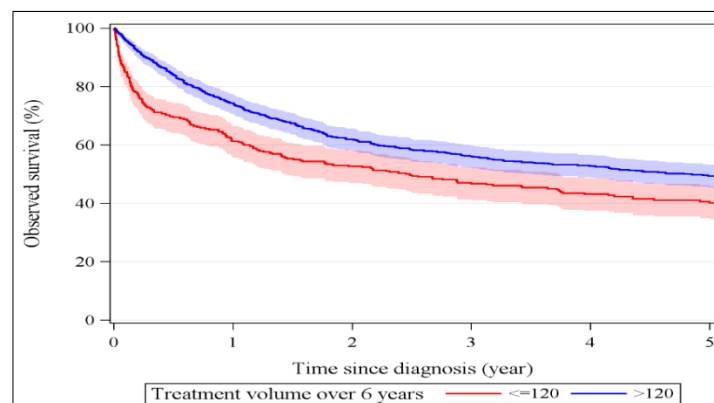
Note: The Kaplan Meier survival function was used.
Source: BCR – IMA

Figure 37 – Distribution of HNSCC patients by main treatment centre, by anatomic site (2009-2014)

Oral cavity
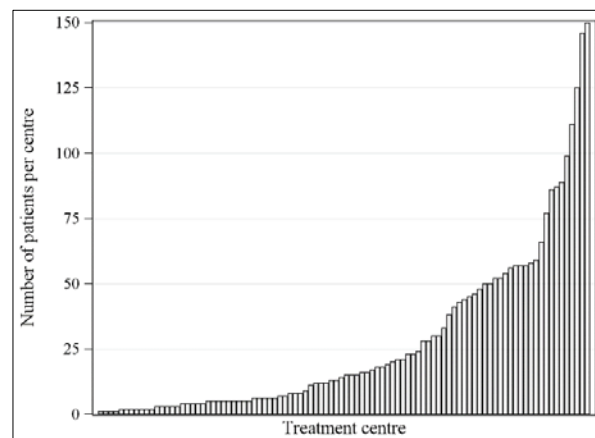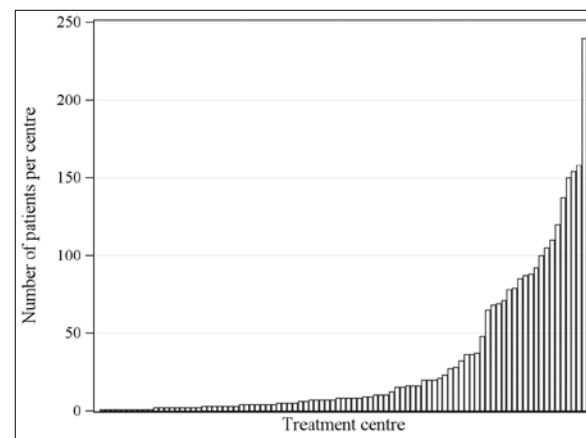
Oropharynx

Hypopharynx
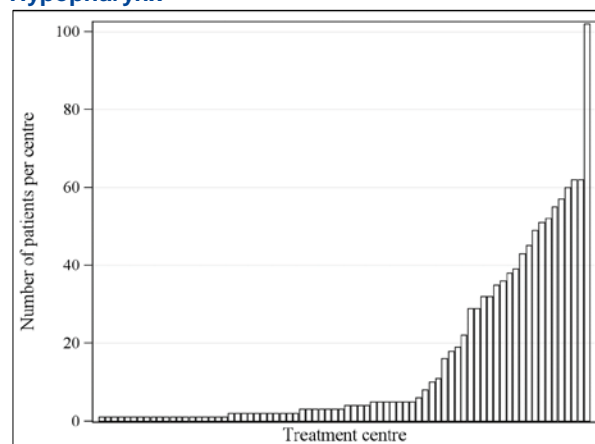
Larynx
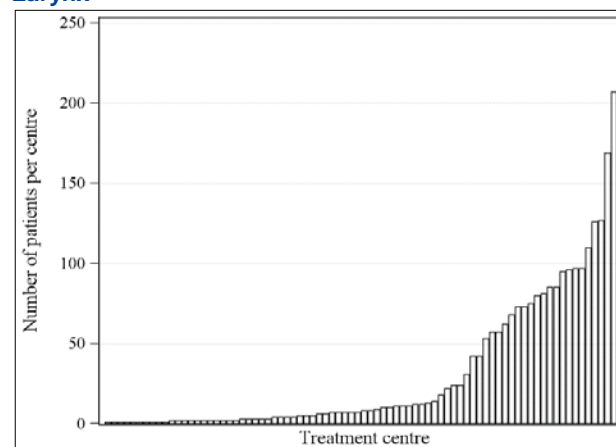
Source: BCR – IMA

Institutional experience: analysis by main treatment centre – Analyses by anatomic site

Oral cavity SCC

Thirty oral cavity SCC patients could not be assigned to a main treatment centre, leaving 2 635 patients who were treated in 96 main treatment centres (Table 149). The median volume was fifteen oral cavity SCC patients (or somewhat more than two patients per year); a quarter of the centres (Q1) treated not more than five patients with oral cavity SCC over the six year period. The centre size distribution is provided in Figure 37.

Table 149 – Distribution of oral cavity SCC patients by main treatment centre over the six year study period (2009-2014)

Total number of centres	Total number of patients	Minimum	Q1	Median	Q3	Maximum
96	2 635	1	5	14.5	44	150
Average number per year	439	<1	<1	2.4	7.3	25

Q: quartile Source: BCR – IMA

There was no statistically significant association between main treatment volume and observed survival among patients with oral cavity SCC (HR: 1.000, 95% CI: 0.998 - 1.002, p=0.68). This observation may (in part) be explained by the fact that a relatively higher proportion of oral cavity SCC patients with early stage tumours, which are 'easier' to treat with surgery alone and have in itself a better prognosis, were treated in low-volume centres while the proportion of stage IVA-B tumours increased across surgical volume categories (Table 151).

Table 150 – 1-, 2-, and 5-year unadjusted observed survival and median observed survival for oral cavity SCC (2009-2014)

			Observed survival (%, 95% CI)			Median observed survival (years)
	N centres	N patients	1-year	2-year	5-year	
Overall	96	2 635	76.4 (74.7, 78.0)	65.2 (63.4, 67.0)	50.2 (48.2, 52.1)	5.1

Source: BCR – IMA

Table 151 – Proportion of patients with oral cavity SCC by combined stage and surgical volume, over the six year study period (2009-2014)

Characteristics	Surgical volume category over six years (N, %)				
	Total	1-4 patients	5-13 patients	14-36 patients	≥ 37 patients
Overall	1 937	63 (100.0)	178 (100.0)	446 (100.0)	1 250 (100.0)
Combined stage					
I	625 (32.3)	25 (39.7)	69 (38.8)	146 (32.7)	385 (30.8)
II	334 (17.2)	10 (15.9)	25 (14.0)	87 (19.5)	212 (17.0)
III	226 (11.7)	3 (4.8)	23 (12.9)	51 (11.4)	149 (11.9)
IVA-B	611 (31.5)	14 (22.2)	32 (18.0)	128 (28.7)	437 (35.0)
X	141 (7.3)	11 (17.5)	29 (16.3)	34 (7.6)	67 (5.4)

Source: BCR – IMA

Oropharyngeal SCC

After the exclusion of 19 patients who could not be assigned to a main treatment centre, 2 726 patients who were treated in 91 main treatment centres were included in the analyses (Table 152). Half of the centres treated eight or less patients with oropharyngeal SCC over the six year study period; three quarters of the centres treated on average six or less patients with oropharyngeal SCC a year. The centre size distribution is provided in Figure 37.

Table 152 – Distribution of oropharyngeal SCC patients by main treatment centre over the six year study period (2009-2014)

Total number of centres	Total number of patients	Minimum	Q1	Median	Q3	Maximum
91	2 726	1	3	8	36	240
Average number per year	454	<1	<1	1.3	6	40

Q: quartile; Source: BCR – IMA

Patients with oropharyngeal SCC who were treated in high-volume centres[o] had a statistically significantly higher chance of survival than patients who were treated in low-volume centres (Table 153).

To take the case-mix of hospitals into account, a Cox proportional hazard model was developed; the optimal knot for the piecewise linear volume association was at forty patients. These analyses revealed that the hazard to die of any cause decreased on average with 1.5% per increase of one additionally treated patient below the break point of forty patients (HR: 0.985, 95% CI: 0.979 - 0.992, p<0.0001). Above this threshold, there was no further significant decrease in hazard (HR: 1.000, 95% CI: 0.998 - 1.002, p=0.99). Using this cut-off of forty patients with oropharyngeal SCC over six years, only twenty centres could be regarded as high-volume centres.

Further analyses revealed interactions between volume and combined stage on observed survival in patients with oropharyngeal SCC: there was a significant association between main treatment volume and observed survival for combined stages III and IVA-B below a volume of forty patients (Table 154).

Table 153 – 1-, 2-, and 5-year unadjusted observed survival and median observed survival for oropharyngeal SCC, by main treatment volume (2009-2014)

	N centres	N patients	Observed survival (%, 95% CI) 1-year	2-year	5-year	Median observed survival (years)	p-value*
Overall	91	2 726	74.5 (72.8, 76.1)	61.6 (59.7, 63.4)	44.9 (43.0, 46.9)	3.8	
Main treatment volume							0.0018
≤ 40 patients over 6 years	71	622	66.4 (62.5, 69.9)	57.3 (53.3, 61.1)	42.3 (38.2, 46.3)	3.1	
> 40 patients over 6 years	20	2 104	76.9 (75.0, 78.6)	62.8 (60.7, 64.9)	45.7 (43.5, 47.9)	3.9	

* p-value applies to the log-rank test between the survival curves.
Source: BCR – IMA

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[o] In order to distinguish low versus high volume centres for the unadjusted survival analyses, the threshold ('knot') defined in the Cox proportional hazard model was used, i.e. forty patients over the six year study period.

Table 154 – Estimated HRs for all-cause death, oropharyngeal SCC patients, site-specific volume, by combined stage (2009-2014)

Characteristic	HR	95% CI	p-value
Treatment volume, stage I, ≤40	0.996	(0.975, 1.017)	0.6953
Treatment volume, stage I, >40	1.000	(0.995, 1.004)	0.8976
Treatment volume, stage II, ≤40	0.996	(0.975, 1.018)	0.7094
Treatment volume, stage II, >40	0.999	(0.995, 1.003)	0.6734
Treatment volume, stage III, ≤40	0.979	(0.963, 0.996)	0.0134
Treatment volume, stage III, >40	1.002	(0.999, 1.005)	0.2680
Treatment volume, stage IVA-B, ≤40	0.982	(0.973, 0.991)	<0.0001
Treatment volume, stage IVA-B, >40	1.000	(0.998, 1.002)	0.8816
Treatment volume, stage IVC, ≤40	0.996	(0.979, 1.015)	0.6944
Treatment volume, stage IVC, >40	0.998	(0.993, 1.003)	0.4507
Treatment volume, stage X, ≤40	0.979	(0.965, 0.995)	0.0080
Treatment volume, stage X, >40	1.001	(0.997, 1.005)	0.6797

Source: BCR – IMA

Hypopharyngeal SCC

Only five patients with hypopharyngeal SCC could not be assigned to a main treatment centre, leaving 1 132 patients who were treated in 76 main treatment centres for the analyses (Table 155). Half of the centres treated less than one patient with hypopharyngeal SCC a year, three quarters of the centres about four or less patients per year. The centre size distribution is provided in Figure 37.

Table 155 – Distribution of hypopharyngeal SCC patients by main treatment centre over the six year study period (2009-2014)

Total number of centres	Total number of patients	Minimum	Q1	Median	Q3	Maximum
76	1 132	1	1	3.5	25	102
Average number per year	188	<1	<1	<1	4.2	17

Q: quartile
Source: BCR – IMA

As is presented in Table 156, patients with hypopharyngeal SCC who were treated in low-volume centres [p] had a statistically significantly lower chance of survival than patients who were treated in high-volume centres. The median observed survival for the first group was only 0.6 years while it was nearly four times higher for patients taken care of in high-volume centres.

For this anatomic site, the optimal knot for the piecewise linear volume association was at ten patients. The adjusted analyses revealed that the hazard to die of any cause decreased on average with 9.4% per increase of one additionally treated patient below a volume of ten patients (HR: 0.906,

95% CI: 0.869 - 0.945, p<0.0001); above the volume of ten no further decrease in hazard was observed (HR: 1.001, 95% CI: 0.996 - 1.006, p=0.73). When ten patients with hypopharyngeal SCC over six years is applied as cut-off, only 24 centres could be regarded as high-volume centres.

Just like the oropharyngeal SCC group, additional analyses revealed a significant association between main treatment volume and observed survival for combined stages III and IVA-B below a volume of ten patients (Table 157).

Table 156 – 1-, 2-, and 5-year unadjusted observed survival and median observed survival for hypopharyngeal SCC, by main treatment volume (2009-2014)

	N centres	N patients	HR (95% CI)	Observed survival (%, 95% CI)			Median observed survival (years)	p-value*
				1-year	2-year	5-year		
Overall	76	1 132		65.7 (62.9, 68.4)	49.8 (46.8, 52.7)	30.9 (28.0, 33.7)	2.0	
Main treatment volume								<0.0001
≤ 10 patients over 6 years	52	138	0.906 (0.869, 0.945)	38.4 (30.3, 46.4)	26.1 (19.1, 33.6)	15.0 (9.3, 22.0)	0.6	
> 10 patients over 6 years	24	994	1.001 (0.996, 1.006)	69.5 (66.5, 72.3)	53.1 (49.9, 56.1)	33.1 (30.0, 36.1)	2.2	

* p-value applies to the log-rank test between the survival curves.
Source: BCR – IMA

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[p]   In order to distinguish low versus high volume centres for the unadjusted survival analyses, the threshold ('knot') defined in the Cox proportional hazard model was used, i.e. ten patients over the six year study period.

Table 157 – Estimated HRs for all-cause death, hypopharyngeal SCC patients, site-specific volume, by combined stage (2009-2014)

Characteristics	HR	95% CI	p-value
Treatment volume, stage I, ≤10	0.999	(0.790, 1.264)	0.9949
Treatment volume, stage I, >10	1.016	(0.988, 1.043)	0.2645
Treatment volume, stage II, ≤10	0.856	(0.681, 1.077)	0.1849
Treatment volume, stage II, >10	0.998	(0.982, 1.014)	0.7828
Treatment volume, stage III, ≤10	0.872	(0.782, 0.972)	0.0139
Treatment volume, stage III, >10	0.997	(0.987, 1.007)	0.5305
Treatment volume, stage IVA-B, ≤10	0.898	(0.845, 0.954)	0.0005
Treatment volume, stage IVA-B, >10	1.003	(0.997, 1.009)	0.3639
Treatment volume, stage IVC, ≤10	0.932	(0.848, 1.024)	0.1412
Treatment volume, stage IVC, >10	1.001	(0.990, 1.013)	0.8053
Treatment volume, stage X, ≤10	0.887	(0.807, 0.974)	0.0122
Treatment volume, stage X, >10	0.997	(0.985, 1.010)	0.6616

Source: BCR – IMA

Laryngeal SCC

Sixteen patients with laryngeal SCC could not be included in the analyses as they could not be assigned to a main treatment centre. Also in this patient group, the dispersion of care was crystal clear: three quarter of the centres treated less than ten patients with laryngeal SCC a year (Table 158). The centre size distribution is provided in Figure 37.

Table 158 – Distribution of laryngeal SCC patients by main treatment centre over the six year study period (2009-2014)

Total number of centres	Total number of patients	Minimum	Q1	Median	Q3	Maximum
81	2 682	1	2	8	57	252
Average number per year	447	<1	<1	1.3	9.5	42

Q: quartile
Source: BCR – IMA

Patients with laryngeal SCC who were treated in high-volume centres [q] had a median observed survival time that was six years longer than their peers who were taken care of in low-volume centres (Table 159).

For this anatomic site, a knot at ten patients was selected in the Cox regression model. The hazard to die of any cause decreased significantly below a volume of ten patients (HR: 0.884, 95% CI: 0.846 - 0.923, p<0.0001), but above that volume no further decrease in hazard was observed (HR=0.999, 95% CI: 0.997 - 1.000, p=0.07). Over the six year period, more than half of the centres could be considered as low-volume centres.

Stratified analyses by combined stage revealed a significant association between main treatment volume and observed survival for combined stage IVA-B below a critical volume of ten patients (Table 160).

Table 159 – 1-, 2-, and 5-year unadjusted observed survival and median observed survival for laryngeal SCC, by main treatment volume (2009-2014)

	N centres	N patients	Observed survival (%, 95% CI) 1-year	2-year	5-year	Median observed survival (years)	p-value*
Overall	81	2 682	83.8 (82.4, 85.2)	74.9 (73.3, 76.5)	60.7 (58.7, 62.5)	8.0	
Main treatment volume							<0.0001
≤ 10 patients over 6 years	45	170	62.1 (54.4, 69.0)	52.0 (44.2, 59.2)	40.4 (32.9, 47.9)	2.3	
> 10 patients over 6 years	36	2 512	85.3 (83.9, 86.6)	76.5 (74.8, 78.1)	62.0 (60.0, 64.0)	8.2	

* p-value applies to the log-rank test between the survival curves.
Source: BCR – IMA

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[q]　In order to distinguish low versus high volume centres for the unadjusted survival analyses, the threshold ('knot') defined in the Cox proportional hazard model was used, i.e. ten patients over the six year study period.

Table 160 – Estimated HRs for all-cause death, laryngeal SCC patients, site-specific volume, by combined stage (2009-2014)

Characteristics	HR	95% CI	p-value
Treatment volume, stage I, ≤10	0.930	(0.822, 1.052)	0.2508
Treatment volume, stage I, >10	0.998	(0.995, 1.001)	0.1212
Treatment volume, stage II, ≤10	0.868	(0.748, 1.008)	0.0635
Treatment volume, stage II, >10	0.999	(0.996, 1.002)	0.5056
Treatment volume, stage III, ≤10	0.943	(0.780, 1.140)	0.5414
Treatment volume, stage III, >10	0.998	(0.995, 1.000)	0.0703
Treatment volume, stage IVA-B, ≤10	0.815	(0.750, 0.886)	<0.0001
Treatment volume, stage IVA-B, >10	0.999	(0.997, 1.001)	0.3507
Treatment volume, stage IVC, ≤10	0.927	(0.820, 1.048)	0.2271
Treatment volume, stage IVC, >10	0.999	(0.993, 1.005)	0.7645
Treatment volume, stage X, ≤10	0.880	(0.816, 0.950)	0.0010
Treatment volume, stage X, >10	0.999	(0.996, 1.003)	0.7201

Source: BCR – IMA

ANALYSES BY TREATMENT TYPE – SURGICAL VOLUME

Table 161 – Estimated HRs for all-cause death, all HNSCC patients, all HNSCC surgical volume, by anatomic site (2009-2014)

Characteristics	HR	95% CI	p-value
Surgical volume, Oral cavity	1.000	(0.998, 1.001)	0.5554
Surgical volume, Oropharynx	1.000	(0.998, 1.002)	0.8873
Surgical volume, Hypopharynx	1.000	(0.996, 1.004)	0.9484
Surgical volume, Larynx	0.998	(0.996 1.000)	0.0185

Source: BCR – IMA

Table 162 – Estimated HRs for all-cause death, all HNSCC patients, all HNSCC <u>surgical volume</u>, by combined stage (2009-2014)

Characteristics	HR	95% CI	p-value
Surgical volume, stage I	0.997	(0.995, 1.000)	0.0287
Surgical volume, stage II	0.999	(0.997, 1.002)	0.5245
Surgical volume, stage III	0.997	(0.995, 1.000)	0.0375
Surgical volume, stage IVA-B	1.000	(0.999, 1.002)	0.5476
Surgical volume, stage X	0.998	(0.995, 1.002)	0.3096

Source: BCR – IMA

ANALYSES BY TREATMENT TYPE – RADIOTHERAPY VOLUME

Table 163 – Estimated HRs for all-cause death, all HNSCC patients, all HNSCC <u>radiotherapy volume</u>, by anatomic site (2009-2014)

Characteristics	HR	95% CI	p-value
RT volume, oral cavity	1.001	(1.000, 1.003)	0.0524
RT volume, oropharynx	1.000	(0.999, 1.001)	0.8557
RT volume, hypopharynx	1.000	(0.999, 1.001)	0.6504
RT volume, larynx	0.998	(0.999 1.0001	0.7396

Source: BCR – IMA

Table 164 – Estimated HRs for all-cause death, all HNSCC patients, all HNSCC <u>radiotherapy volume</u>, by combined stage (2009-2014)

Characteristic	HR	95% CI	p-value
RT volume, stage I	1.000	(0.998, 1.001)	0.6570
RT volume, stage II	1.000	(0.999, 1.002)	0.9205
RT volume, stage III	1.000	(0.999, 1.001)	0.7328
RT volume, stage IVA-B	1.000	(0.999, 1.001)	0.7165
RT volume, stage X	1.002	(1.000, 1.003)	0.0207

Source: BCR – IMA

Results - Association between hospital volume and 30-day post-treatment mortality

SURGICAL VOLUME

Table 165 – Estimated ORs for 30-day <u>post-operative</u> mortality, all HNSCC patients, all HNSCC surgical volume, by anatomic site (2009-2014)

Characteristic	OR	95% CI	p-value
Surgical volume, oral cavity	0.998	(0.993, 1.003)	0.8948
Surgical volume, oropharynx	0.999	(0.990, 1.008)	0.9115
Surgical volume, hypopharynx	1.012	(0.993, 1.031)	0.0698
Surgical volume, larynx	0.992	(0.984, 0.999)	0.2725

Source: BCR – IMA

RADIOTHERAPY VOLUME

Table 166 – Estimated ORs for 30-day post-radiotherapy mortality, all HNSCC patients, all HNSCC radiotherapy volume, by anatomic site (2009-2014)

Characteristic	OR	95% CI	p-value
RT volume, oral cavity	1.003	(0.999, 1.007)	0.1873
RT volume, oropharynx	1.001	(0.999, 1.004)	0.3519
RT volume, hypopharynx	1.001	(0.997, 1.004)	0.6390
RT volume, larynx	1.000	(0.996, 1.003)	0.8309

Source: BCR – IMA

International comparison

Table 167 – Impact of hospital volume - International results

Author	Period covered	Country	Results
Systematic review and meta-analysis			
Eskander et al., 2014[117]	1947-2013	US and Taiwan	Seventeen studies included (one case series and sixteen retrospective cohort studies) that focused on patients with head and neck cancer who had undergone surgery (ablative or reconstructive procedures), and/or radiation therapy. Eleven assessed hospital volume, nine assessed surgeon volume, and two assessed radiation oncologist volume. All but two studies demonstrated at least one volume-outcome relationship in head and neck cancer. The two studies that did not find a volume-outcome relationship mixed different cancer types or had a relatively small sample size.
			Only two out of eight studies assessing **short-term survival outcomes** (in-hospital death, 30-day mortality or 99-day mortality) demonstrated a hospital volume-outcome relationship.
			The results of five studies evaluating hospital volume and **long-term overall survival** were meta-analysed and demonstrated a random effects model pooled HR of 0.886 (95% CI: 0.820 - 0.956) **favouring high-volume hospitals**.
			All five studies assessing **physician** volume found significant relationships with long-term overall survival: in oral cavity resection, there was a better 5-year overall survival in patients treated by **high-volume surgeons**.
Primary studies & audit reports			
David et al., 2017[124]	2004-2012	US	Retrospective population-based study with 46 567 patients diagnosed from 2004 through 2012 with **stage III – stage IVB** SCC of the oropharynx, hypopharynx and larynx, undergoing definitive **radiotherapy**. Multivariable analyses revealed that treatment at a **high-volume centre** (i.e. top 1% of centres by the number of patients, HR: 0.798, 95% CI: 0.753 - 0.845) and treatment at an **academic facility** (HR: 0.897; 95% CI: 0.871 - 0.923) were independently associated with improved overall survival.
de Ridder et al., 2017[114]	2008	The Netherlands	In total, 2 094 newly diagnosed patients with head and neck cancer were included. A **lower hazard of dying with increasing hospital volume** was observed, after correction for age, gender and stage (HR of 0.98 per 25 patients, 95% CI: 0.95 - 1.00). However, a volume-outcome relationship was not confirmed in analyses restricted by subsite, probably due to the lower number of patients by subsite in combination with the low effect for volume. No separate analyses were performed for surgical or RT volume, neither for surgeon or radiologist volume.
Boero et al., 2016[146]	2000-2009	US	Population-based study to evaluate the influence of radiation oncologist experience on outcomes in patients with HNC treated with **IMRT** compared with patients with HNC treated with conventional radiation therapy; Medicare claims data of 6 212 patients (> 65 years old) were evaluated. Among 2 242 patients receiving IMRT, those treated by **higher-volume radiation oncologists** had decreased all-cause mortality (HR: 0.79, 95% CI: 0.67 - 0.94). For patients treated with conventional radiation therapy, there was no significant impact on all-cause mortality from provider experience (HR: 0.95, 95% CI: 0.87 - 1.04).

Author	Period covered	Country	Results
Wuthrick et al., 2015[119]	2002-2005	US and Canada[r]	The effect of **institutional experience** on overall survival in patients with stage III or IV HNSCC was investigated within a randomized trial of the Radiation Therapy Oncology Group (RTOG 0129[r]) which compared cisplatin concurrent with standard versus accelerated fractionation radiotherapy. The study included 471 patients; as a surrogate for institutional expertise, institutional accrual volume to 21 HNC clinical trials conducted by the RTOG during the 5-year period (July 30, 1997, to July 29, 2002) immediately before the activation of RTOG 0129 was used. **Patients at historically low accruing centres (HLACs) had significantly worse OS** (5 years: 51.0% vs. 69.1%; HR: 1.67; 95% CI: 1.21 - 2.31) when compared with historically high accruing centres (HHACs). Patients treated at HLACs also had **significantly worse Progression-Free Survival** (5 years: 42.7% vs. 61.8%; HR: 1.64; 95% CI: 1.22 - 2.20). Radiotherapy protocol deviations were higher at HLACs versus HHACs (18% vs. 6%; p<0.001).
Eskander et al., 2014[118]	1993-2010	Ontario (Canada)	A retrospective cohort study to assess whether **surgeon and/or institution resection volume** predicts long-term overall survival; the cohort consisted of 5 720 HNSCC patients. In a crude model that only adjusted for both surgeon and hospital volume (both as continuous variables), both were highly statistically significant, with higher volume predicting improved overall survival (surgeon volume: HR: 0.93, 95% CI: 0.88-0.98; hospital volume: HR: 0.98, 95% CI: 0.97-0.99). However, after controlling for important covariates, **hospital volume** (HR: 0.98, 95% CI: 0.96-1.00), but not surgeon volume, remained statistically significant. For every additional 25 cases performed by an institution, there was a 2% decrease in the Hazard Ratio (p=0.02).

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[r] https://www.rtog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=0129

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