SHORT REPORT

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

- A set of 13 quality indicators covering the diagnosis and treatment of squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx and larynx (Head and neck squamous cell carcinoma, HNSCC) has been developed. These indicators were measured using data from the Belgian Cancer Registry, coupled with the health insurance billing data, hospital discharge data, and vital status data. These indicators can be used to identify areas for quality improvement.

- The results revealed a large dispersion of care: the 9,245 included patients, who were diagnosed with a unique squamous cell carcinoma in the head and neck region in 2009-2014, were treated in 99 different centres. Half of the centres treated four or even less patients per year. HNSCC patients who were treated in high-volume centres (>20 patients/year) had a higher chance to survive than their peers who were treated in low-volume centres (≤20 patients/year), supporting the recommendation to concentrate the management of head and neck cancer patients in reference centres.

- The relative survival was 78.2% at 1 year and decreased to about 55.0% at 5 years, with some variations between the four anatomic sites. International comparison based on data from 2000-2007 showed that the age-standardised 1-year survival in Belgium (data limited to Flanders) is similar to that of neighbouring countries, but the 5-year relative survival slightly below the average for central Europe.

- Post-operative and post-radiotherapy 30-day mortality rates (2.2% and 4%, respectively) were below the target set at 5%, but somewhat higher than those reported in other countries.

- The process indicators related to diagnosis and staging showed substantial room for improvement:
  - The quality of data reporting to the Belgian Cancer Registry is inadequate: clinical and pathological stage information was not reported for 19.5% and 21.6% of patients, respectively;
  - Only 47.6% of patients with an advanced stage cancer (clinical stage III-IV) received a whole-body FDG-PET/CT before their treatment, which is far below the target of ≥90%. Yet, in patients with early stage (clinical stage I-II) HNSCC for whom this exam is not recommended (target ≤5%), no less than 22.9% of patients had a whole-body FDG-PET/CT;
  - The majority of HNSCC patients (82.5%) were staged with MRI and/or CT before the start of the first treatment, yet again the target (90%) was not reached;
  - The delay between diagnostic confirmation and start of first treatment with curative intent showed a great variability between hospitals. In half of the patients, this delay was greater than one month.

- Likewise, the results obtained for all indicators related to the treatment of HNSCC were below the targets set by the experts, and should thus inspire initiatives to change future clinical practice:
  - In early stage HNSCC patients, a single-modality treatment (either surgery or radiotherapy) was offered to 78.1% of intended patients which is close to, but still below the set target (i.e. 80-85%);
  - Only 62.9% of patients with non-metastatic T4a laryngeal cancer underwent a total laryngectomy, which is below the set target (i.e. ≥80%);
Only 48.5% of HNSCC patients ended their radiotherapy within 13 weeks after surgery, which is far below the target set at ≥ 90;

- Concomitant platinum-based chemotherapy was offered to only 58.2% of patients younger than 70 years with locally-advanced stage non-metastatic HNSCC (stage III-IVa-IVb) who had radiotherapy, which is also below the target (i.e. 75-80%);

- 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, was only 32.7%, hence below the target set at 80%;

- Only 56.4% 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%.

- The Belgian Cancer Registry will provide individual feedback reports to all centres, to encourage and support corrective actions to improve the quality of care in HNSCC patients.
## SHORT REPORT

### TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>KEY MESSAGES</td>
<td>1</td>
</tr>
<tr>
<td>SHORT REPORT</td>
<td>3</td>
</tr>
<tr>
<td><strong>1. BACKGROUND</strong></td>
<td>7</td>
</tr>
<tr>
<td>1.1. QUALITY IMPROVEMENT INITIATIVES IN ONCOLOGY</td>
<td>7</td>
</tr>
<tr>
<td>1.2. HEAD AND NECK CANCER, A HETEROGENEOUS GROUP OF MALIGNANCIES AFFECTING VARIOUS SITES WITH DIFFERING PROGNOSIS</td>
<td>7</td>
</tr>
<tr>
<td>1.3. SCOPE</td>
<td>7</td>
</tr>
<tr>
<td>1.4. WHAT THIS STUDY AIMS AT AND DOES NOT AIM AT</td>
<td>7</td>
</tr>
<tr>
<td><strong>2. DATA AND METHODS</strong></td>
<td>8</td>
</tr>
<tr>
<td>2.1. THE DATABASE - A LINKAGE BETWEEN THE BELGIAN CANCER Registry AND ADMINISTRATIVE DATABASES</td>
<td>8</td>
</tr>
<tr>
<td>2.2. THE PATIENTS - DIAGNOSED IN 2009-2014, WITH EXCLUSION OF PATIENTS WITH MULTIPLE AND RECURRENT TUMOURS</td>
<td>9</td>
</tr>
<tr>
<td>2.3. ASSIGNMENT OF PATIENTS TO A CENTRE OF DIAGNOSIS, A CENTRE OF MAIN TREATMENT AND A CENTRE OF FIRST TREATMENT</td>
<td>9</td>
</tr>
<tr>
<td>2.4. CASE-MIX ADJUSTMENT</td>
<td>9</td>
</tr>
<tr>
<td>2.5. IDENTIFICATION AND SELECTION OF POSSIBLE QUALITY INDICATORS</td>
<td>9</td>
</tr>
<tr>
<td>2.6. VALIDATION STUDY AND SUBSEQUENT DATA CHECKS</td>
<td>10</td>
</tr>
<tr>
<td>2.7. STATISTICAL ANALYSES</td>
<td>10</td>
</tr>
<tr>
<td><strong>3. QUALITY OF CARE FOR PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CARCINOMA</strong></td>
<td>11</td>
</tr>
<tr>
<td>3.1. A COHORT OF 9 245 HNSCC PATIENTS DIAGNOSED IN 2009-2014</td>
<td>11</td>
</tr>
<tr>
<td>3.2. MAIN THERAPEUTIC PROCEDURES: RADIOTHERAPY AND SURGERY</td>
<td>13</td>
</tr>
<tr>
<td>3.3. LARGE DISPERSION OF CARE IN BELGIUM</td>
<td>13</td>
</tr>
<tr>
<td>3.4. RESULTS FOR 12 QUALITY INDICATORS</td>
<td>14</td>
</tr>
</tbody>
</table>
3.4.1. Diagnosis and staging......................................................................................................................... 15
3.4.2. Treatment........................................................................................................................................ 18
3.4.3. Safety of care – 30-day mortality after treatment with curative intent........................................... 20
3.4.4. Survival after the diagnosis of HNSCC ......................................................................................... 22
3.5. ASSOCIATION BETWEEN HOSPITAL VOLUME AND SURVIVAL .................................................. 22

4. STRENGTHS AND LIMITATIONS ........................................................................................................ 24

5. CONCLUSIONS AND PERSPECTIVES FOR THE FUTURE .................................................................. 26
   ■ RECOMMENDATIONS ......................................................................................................................... 28
   ■ REFERENCES .......................................................................................................................................... 31
## List of Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>95% CI</td>
<td>95% Confidence Interval</td>
</tr>
<tr>
<td>BCR</td>
<td>Belgian Cancer Registry</td>
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<tr>
<td>cI, cII, etc.</td>
<td>Clinical stage I, clinical stage II, etc.</td>
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<tr>
<td>CCI</td>
<td>Charlson Comorbidity Index</td>
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<tr>
<td>CRT</td>
<td>Chemoradiotherapy</td>
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<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>DW-MRI</td>
<td>Diffusion-weighted magnetic resonance imaging</td>
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<tr>
<td>ENT</td>
<td>Ear, Nose and Throat</td>
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<tr>
<td>FDG-PET(CT)</td>
<td>Positron-emission tomography (computed tomography) with the tracer molecule fluorodeoxyglucose</td>
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<tr>
<td>HNSCC</td>
<td>Head and neck squamous cell carcinoma</td>
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<td>HPV</td>
<td>Human Papilloma Virus</td>
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<tr>
<td>HR</td>
<td>Hazard Ratio</td>
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<tr>
<td>IMA – AIM</td>
<td>Intermutualistic Agency (‘Intermutualistisch Agentschap’ – ‘Agence Intermutualiste’)</td>
</tr>
<tr>
<td>INSZ – NISS</td>
<td>Social security identification number (‘Identificatienummer van de sociale zekerheid’ – ‘Numéro d’identification de la sécurité sociale’)</td>
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<tr>
<td>KCE</td>
<td>Belgian Health Care Knowledge Centre</td>
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<tr>
<td>MDT</td>
<td>Multidisciplinary team meeting (‘Multidisciplinair Oncologisch Consult’ (MOC) – ‘Consultation Oncologique Multidisciplinaire’ (COM))</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic resonance imaging</td>
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<tr>
<td>MZG – RHM</td>
<td>Hospital discharge dataset (‘Minimale Ziekenhuis Gegevens’/Résumé Hospitalier Minimum’)</td>
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<tr>
<td>OR</td>
<td>Odds Ratio</td>
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<tr>
<td>PET/CT</td>
<td>Positron emission tomography/Computed tomography</td>
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<tr>
<td>QI</td>
<td>RT</td>
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<tr>
<td>QI</td>
<td>Quality indicator</td>
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<tr>
<td>TNM</td>
<td>Tumour – Node – Metastasis (i.e. classification of malignant tumours based on tumour size, local metastasis and distant metastasis)</td>
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1. BACKGROUND

1.1. Quality improvement initiatives in oncology

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. The integrative quality improvement system starts with the development and implementation of clinical practice guidelines, followed by the development of a set of indicators. With the set of quality indicators, we aim at measuring the quality of care at the national and hospital level and, most importantly, provide individual feedback to all Belgian hospitals, which can lead to corrective actions to improve the quality of care. So far, the various steps of this improvement cycle have been implemented for rectal (in collaboration with PROCARE), breast, testicular, oesophageal, gastric and lung cancer.1-5

Because head and neck cancer presents an important burden and the management of head and neck cancer is currently very dispersed in Belgium,6 while it requires high specialisation, it was decided that head and neck cancer was the focus of the next quality improvement initiative. In a first step, evidence-based guidelines for the diagnosis and treatment of squamous cell carcinoma of the oral cavity in 2014 and the oropharynx, hypopharynx and larynx in 2015 were published.7, 8 The quality indicators developed for the present study were (partly) based on these guidelines.

1.2. Head and neck cancer, a heterogeneous group of malignancies affecting various sites with differing prognoses

Head and neck cancers are a heterogeneous group of tumour entities, which are anatomically close to each other, but dissimilar in terms of aetiology, histology, and prognosis.9 Typically, head and neck cancers develop in a population with large tobacco and alcohol consumption.10 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.11 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.12

Head and neck cancers occur preferentially in males. In 2015 there were 2 663 new diagnoses of head and neck cancer in Belgium, 73% of them in males.13 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).14 In 2015, the mean age at diagnosis was 64 years.13 In Europe, age-standardised 5-year relative survival is the poorest for hypopharynx (25%), intermediate for oropharynx (39%) and oral cavity (45%) and highest for larynx cancers (59%). With the exception of patients with laryngeal cancer, survival is significantly better in women than in men.9

1.3. 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 as they were not covered in the KCE guidelines. Hence, from here on 'head and neck cancer' should be read as ‘squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx and larynx’.

1.4. 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. In this way areas for quality improvement can be identified. 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? Ultimately, the aim of this study is to improve the quality of care offered to patients affected by head and neck cancers in Belgium.

Many indicators were analysed per hospital, which enables the analysis of the variability between hospitals. This approach also allows to provide individual feedback 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 comparison between individual hospitals as they are extracted from administrative databases originally not intended for quality measurements. Sample sizes were often small, the nomenclature not always clear 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. 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 therefore be regarded as a baseline for follow-up of the quality of care in the future and as a benchmark to evaluate the implementation of the two KCE guidelines.

2. DATA AND METHODS

2.1. The database - a linkage between the Belgian Cancer Registry and administrative databases

The main data source for this project is the Belgian Cancer Registry database, which is linked with

1. health insurance data obtained via the Intermutualistic Agency (IMA – AIM), providing information on diagnostic and therapeutic procedures as well as pharmaceuticals which are reimbursed by sickness funds,

2. hospital discharge data (MZG – RHM) needed to calculate the Adapted Charlson Comorbidity Indexa (CCI) and to obtain the number of days spent in hospital the year before cancer incidence (see 2.4), and with


This linkage is based on the patients’ unique social security number (INSZ – NISS), and has been approved by the Sector Committee of Social Security and of Health (Health Section) of the Belgian Privacy Commission (Sectoraal comité van de Sociale Zekerheid en van de Gezondheid, afdeling gezondheid/Comité sectoriel de la Sécurité Sociale et de la Santé, section santé).15, 16

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One of the validated instruments to measure comorbidity in HNSCC patients is the Charlson Comorbidity Index (CCI), which uses the primary and secondary diagnoses registered at hospital admission. For the purpose of the present study, the original CCI has been adapted slightly; the details are described in the Scientific Report section 3.3.5). When in this document ‘Charlson Comorbidity Index adapted’ is written, this should be read as: ‘the Charlson Comorbidity Index after adaptation as is described in section 3.3.5’.
2.2. The patients - diagnosed in 2009-2014, with exclusion of patients with multiple and recurrent tumours

Among the 15,339 patients diagnosed with a head and neck cancer in the period 2009-2014, 12,756 were diagnosed with a squamous cell carcinoma (SCC) of the oral cavity, oropharynx, hypopharynx or larynx. IMA – AIM data were available for 98.3% of these patients. 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 to treat the head and neck squamous cell carcinoma (HNSCC) and not another malignancy. After additional exclusion of those patients who died at the date of diagnosis or who were lost to follow-up, a final cohort of 9,245 patients with a unique HNSCC was included. The vital status of these patients was followed up until 14 December 2017, allowing a follow-up of at least three years for the majority of patients.

2.3. Assignment of patients to a centre of diagnosis, a centre of main treatment and a centre of first treatment

For the benchmarking between hospitals, the volume-outcome analyses as well as the individual feedback to hospitals, it is essential to identify in which hospital patients received their diagnostic and therapeutic care. In other words, each patient had to be assigned to a centre, also when a patient was taken care of in more than one hospital. Depending on the quality indicator, benchmarking between hospitals was done based on the centre of main treatment, the centre of first treatment, the centre of surgery, the centre of radiotherapy or the diagnostic centre; hence several assigning algorithms were constructed. For the detailed descriptions of these algorithms, the reader is referred to the Scientific Report, section 3.4.

2.4. Case-mix adjustment

When outcomes between providers (e.g. oncologists, surgeons, radiotherapists or more globally hospitals) who treat patients with different patient and tumour characteristics are compared, case-mix adjustment is certainly indicated. Without this adjustment the analysis may be misleading. Whenever relevant and possible, the following confounders were taken into account: gender, age group at diagnosis, WHO performance status, combined stage\(^{2}\), the adapted Charlson Comorbidity Index and the number of previous inpatient bed days\(^{3}\). Sadly, neither the BCR nor the IMA – AIM database contained data on other well-established confounding factors, like HPV infection, the socio-economic background of the patient, alcohol consumption and smoking. However, the Charlson Comorbidity Index was used, which includes some pathologies that are also associated with alcohol consumption and smoking (e.g. peripheral vascular disease, chronic pulmonary disease, liver disease); a better proxy was not possible.

2.5. Identification and selection of possible quality indicators

An initial long list of 176 quality indicators (QIs) was composed of QIs selected from published papers and quality reports, supplemented with QIs derived from the recommendations of the KCE guidelines and QIs suggested by the experts. Wherever possible, QIs that referred to the same concept were merged and indicators that were not in agreement with Belgian clinical recommendations were adjusted or removed. This led to an intermediate list of 107 QIs, which were scored by a panel of 11 clinical experts (see colophon), BCR and KCE for their relevance on a 1-5 scale. The in- and exclusion of QIs was further discussed during two consensus meetings with the clinical experts, BCR and KCE. The 33 remaining QIs 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. Finally, 13 measurable QIs were retained and form the basis of this report. Of these, 10 QIs

\(^{2}\) 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.

\(^{3}\) The number of previous inpatient bed days is another parameter which was taken into account in case-mix adjustment; it refers to the number of days spent in a hospital by the patient within 12 months before start date of cancer treatment as is described in Scientific Report section 3.3.5.
assessed processes of care and 2 QIs outcomes of care; the results are described in section 3.4. In the elaboration of the 13th QI, i.e. volume of patients with HNSCC treated (a QI assessing structure), emphasis was laid on the association between volume and outcomes (survival and 30-day mortality; see section 3.5). Whenever applicable, a target was defined by expert consensus before the analysis of the QI.

2.6. Validation study and subsequent data checks

In order to assess the concordance between the diagnostic and therapeutic procedures identified in the administrative database and the information available in the hospitals (e.g. medical files, financial data, considered as ‘gold standard’) and to assess the correctness of the algorithm to assign patients to the centre of main treatment (cf. supra), a validation study was performed. This data check was conducted in sixteen hospitals, geographically distributed across the country, including academic and non-academic centres, as well as ‘low and high head and neck cancer volume centres’. Upfront it was agreed that the concordance between the administrative database and the information available in the respective hospitals should be at least 95%.

The validation study led to a further optimization of the assignment algorithm and of the nomenclature selections to define diagnostic and therapeutic procedures which are used for the calculation of the quality indicators (for more details, the reader is referred to the Scientific Report, section 3.5). As the results were not yet convincing for surgery with curative intent, it was checked whether a better concordance could be achieved with hospital discharge data (MZG – RHM). From these additional analyses we learned that the concordance was even lower than with the linked BCR – IMA database and so this approach had no added value and was abandoned.

Lastly, because of the difficulties with the identification of surgical procedures with curative intent in T1-T2 hypopharyngeal and laryngeal SCC, the IMA – AIM data for these tumour types were compared with the pathology reports, leading to an acceptable concordance for T1-T2 laryngeal SCC (96%), but not for T1-T2 hypopharyngeal SCC (i.e. 88%).

As for the clinical experts the exclusion of T1-T2 hypopharyngeal SCC was not an option, it was agreed to accept this larger deviation for small hypopharyngeal SCC, as numbers are low and no alternative approaches were available. The lower concordance than aspired calls for a careful interpretation of these results.

2.7. Statistical analyses

Simple descriptive statistics were used to report results at the national level. The variability between centres is presented in funnel plots (e.g. Figure 3, see Box 1), scatter plots (e.g. Figure 2 and Figure 5) and forest plots (e.g. Figure 6).

Post-treatment mortality at 30, 60 and 90 days was calculated as the ratio of the patients who died within the specific time period and the number of patients alive at time zero (see section 1.1.1). The post-treatment mortality at 30 days was further modelled with logistic regression, taking into account the baseline patient case mix variables. Differences between hospitals were evaluated by estimating the odds ratio (OR) for post-operative death adjusted for patient case mix and displayed in a forest plot (Figure 6). The 1-, 2- and 5-year overall and relative survival probabilities were estimated using the Kaplan–Meier and the Ederer II methods, respectively (see section 1.1.1). The relation between hospital volume and observed survival since diagnosis was then assessed with Cox proportional hazard models adjusted for potential confounders.

The technical fiches and analysis methods were agreed and finalised before the analyses were started.

d T1-T2 hypopharyngeal and laryngeal SCC were not included in the validation study as at that time of the study, it was judged not possible yet to identify the right surgical codes in the administrative database (more precisely, it was not possible to disentangle diagnostic procedures from procedures performed with curative intent).

e 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).
Box 1 – Funnel plot, a useful tool to assess the variability between centres

In a funnel plot each hospital’s result is plotted against a measure of its precision (often the hospital volume, but not always), with prediction limits of 95% and 99% around the overall result at the national level (e.g. Figure 3). In this way, funnel plots are a useful tool to compare the variability between centres with the sampling variability one would expect if all centres have the same underlying population value. Funnel plots are used in quality assessments as this presentation avoids spurious ranking of hospitals.23 Because the underreporting of TNM stage information may bias the results (see section 1.1.1), 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 (e.g. Figure 2 – Figure 4).

3. QUALITY OF CARE FOR PATIENTS WITH HEAD AND NECK SQUAMOUS CELL CARCINOMA

3.1. A cohort of 9 245 HNSCC patients diagnosed in 2009-2014

In the six year study period 9 245 patients were diagnosed with squamous cell carcinoma of the oral cavity, oropharynx, hypopharynx or larynx. Three quarters of included patients were men; the mean age at diagnosis was 62.3 years (Table 1). Sixty percent of the 8 812 patients with available hospital discharge data had no recorded comorbidities. For those who had comorbidities, the most prevalent were chronic pulmonary disease (19.4%), diabetes without chronic complications (8.0%) and peripheral vascular disease (5.6%). Two thirds of the patients were diagnosed with an advanced (combined) stage of the tumour (III-IV, 64.7%). However, this proportion varied considerably among the different anatomic sites: from 46.7% for laryngeal SCC to 88.7% for hypopharyngeal SCC (Table 1). For more details the reader is referred to the Scientific Report, section 4.
<table>
<thead>
<tr>
<th>Gender</th>
<th>Total (N 9 245)</th>
<th>Oral cavity (N 2 665)</th>
<th>Oropharynx (N 2 745)</th>
<th>Hypopharynx (N 1 137)</th>
<th>Larynx (N 2 698)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>N 7 017 75.9%</td>
<td>N 1 770 66.4%</td>
<td>N 1 998 72.8%</td>
<td>N 974 85.7%</td>
<td>N 2 275 84.3%</td>
</tr>
<tr>
<td>Female</td>
<td>N 2 228 24.1%</td>
<td>N 895 33.6%</td>
<td>N 747 27.2%</td>
<td>N 163 14.3%</td>
<td>N 423 14.3%</td>
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<table>
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<tr>
<th>Age group</th>
<th>Total (N 9 245)</th>
<th>Oral cavity (N 2 665)</th>
<th>Oropharynx (N 2 745)</th>
<th>Hypopharynx (N 1 137)</th>
<th>Larynx (N 2 698)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean, SD (years)</td>
<td>62.3 SD 1.1</td>
<td>62.2 SD 12.4</td>
<td>60.8 SD 10.1</td>
<td>61.4 SD 9.5</td>
<td>64.3 SD 10.8</td>
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<table>
<thead>
<tr>
<th>Adapted Charlson Comorbidity Index</th>
<th>Total (N 9 245)</th>
<th>Oral cavity (N 2 665)</th>
<th>Oropharynx (N 2 745)</th>
<th>Hypopharynx (N 1 137)</th>
<th>Larynx (N 2 698)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0*</td>
<td>N 5 359 60.8%</td>
<td>N 1 548 61.8%</td>
<td>N 1 598 61.6%</td>
<td>N 609 55.4%</td>
<td>N 1 604 61.3%</td>
</tr>
<tr>
<td>1-2*</td>
<td>N 2 747 31.2%</td>
<td>N 777 31.0%</td>
<td>N 769 29.7%</td>
<td>N 393 35.8%</td>
<td>N 808 30.9%</td>
</tr>
<tr>
<td>3-4*</td>
<td>N 557 6.3%</td>
<td>N 145 5.8%</td>
<td>N 183 7.1%</td>
<td>N 69 6.3%</td>
<td>N 160 6.1%</td>
</tr>
<tr>
<td>&gt;4*</td>
<td>N 149 1.7%</td>
<td>N 35 1.4%</td>
<td>N 43 1.7%</td>
<td>N 28 2.5%</td>
<td>N 43 1.6%</td>
</tr>
<tr>
<td>No data available</td>
<td>N 433</td>
<td>N 152</td>
<td>N 38</td>
<td>N 83</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Combined stage§</th>
<th>Total (N 9 245)</th>
<th>Oral cavity (N 2 665)</th>
<th>Oropharynx (N 2 745)</th>
<th>Hypopharynx (N 1 137)</th>
<th>Larynx (N 2 698)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reported:</td>
<td>N 8 250 89.2%</td>
<td>N 2 382 89.4%</td>
<td>N 2 498 91.0%</td>
<td>N 1 041 91.6%</td>
<td>N 2 329 86.3%</td>
</tr>
<tr>
<td>I*</td>
<td>N 1 794 21.7%</td>
<td>N 677 28.4%</td>
<td>N 221 8.8%</td>
<td>N 43 4.1%</td>
<td>N 853 36.6%</td>
</tr>
<tr>
<td>II*</td>
<td>N 1 119 13.6%</td>
<td>N 392 16.5%</td>
<td>N 264 10.6%</td>
<td>N 74 7.1%</td>
<td>N 389 16.7%</td>
</tr>
<tr>
<td>III*</td>
<td>N 1 257 15.2%</td>
<td>N 288 12.1%</td>
<td>N 409 16.4%</td>
<td>N 174 16.7%</td>
<td>N 386 16.6%</td>
</tr>
<tr>
<td>IVA*</td>
<td>N 3 408 41.3%</td>
<td>N 919 38.6%</td>
<td>N 1 306 52.3%</td>
<td>N 570 54.8%</td>
<td>N 613 26.3%</td>
</tr>
<tr>
<td>IVB*</td>
<td>N 327 4.0%</td>
<td>N 50 2.1%</td>
<td>N 159 6.4%</td>
<td>N 91 8.7%</td>
<td>N 27 1.2%</td>
</tr>
<tr>
<td>IVC*</td>
<td>N 345 4.2%</td>
<td>N 56 2.4%</td>
<td>N 139 5.6%</td>
<td>N 89 8.5%</td>
<td>N 61 2.6%</td>
</tr>
<tr>
<td>X (missing)</td>
<td>N 995 10.8%</td>
<td>N 283 10.6%</td>
<td>N 247 9.0%</td>
<td>N 96 8.4%</td>
<td>N 369 13.7%</td>
</tr>
</tbody>
</table>

SD: Standard deviation; § 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; * The % for the CCI adapted were calculated excluding the missing data, likewise stages I, II, III and IVA, IVB, IVC were computed excluding the X category.

Source: BCR – IMA – MZG
3.2. Main therapeutic procedures: radiotherapy and surgery

Nearly half of the HNSCC cohort was treated with primary radiotherapy (RT), with or without systemic therapy (N=4 666) and another large group with surgery with curative intent, with or without (neo)adjuvant therapy (N=3 518). Clear differences were observed 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.

3.3. Large dispersion of care in Belgium

In 2009 there were 109 acute hospitals in Belgium; this number dropped to 104 by 2014. The 9 175 HNSCC patients who could be assigned to a main treatment centre (see section 2.3) were treated in 99 different centres (Table 2). The median treatment centre volume was 25 unique patients over six years’ time, 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 (see Table 2, Figure 1). Another striking example of the dispersion of head and neck cancer care in Belgium: the 73 total laryngectomies in patients with non-metastatic T4a laryngeal cancer (cf. infra) were performed in 33 centres. Only three centres performed at least ten laryngectomies over the six year study period. Important to note here is that these volume data are solely based on patients with a unique HNSCC tumour; for methodological reasons the 3 287 patients with multiple invasive tumours were excluded from the analyses (cf. section 2.2).

Table 2 – Distribution of HNSCC patients by main treatment centre over a six year period (2009-2014)

<table>
<thead>
<tr>
<th>Total number of centres</th>
<th>Total number of patients</th>
<th>Min</th>
<th>Q1</th>
<th>Median</th>
<th>Q3</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>99</td>
<td>9 175</td>
<td>1</td>
<td>10</td>
<td>25</td>
<td>115</td>
<td>744</td>
</tr>
<tr>
<td>Average number per year</td>
<td>1 529</td>
<td>&lt;1</td>
<td>1.6</td>
<td>4.2</td>
<td>19.2</td>
<td>124</td>
</tr>
</tbody>
</table>

Q: quartile
Source: BCR – IMA
### 3.4. Results for 12 quality indicators

An overview of the main results of 12 QIs is provided in Table 3 which are discussed in the following paragraphs. Given the importance of the volume-outcome analyses, these results are discussed in a dedicated section (section 3.5).

**Table 3 – Overview of 12 quality indicators for the diagnosis and treatment of HNSCC patients diagnosed in 2009-2014**

<table>
<thead>
<tr>
<th>ID</th>
<th>Quality Indicator</th>
<th>Result (%, 95% CI)</th>
<th>Target (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DS-1</td>
<td>Median time between incidence date and start of first treatment with curative intent</td>
<td>32 days (IQR: 19 - 46)</td>
<td>--</td>
</tr>
<tr>
<td>DS-2</td>
<td>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</td>
<td>82.5</td>
<td>90</td>
</tr>
<tr>
<td>DS-3</td>
<td>A. Proportion of patients with HNSCC who have their cTNM stage reported to the Belgian Cancer Registry (BCR)</td>
<td>80.5</td>
<td>95</td>
</tr>
<tr>
<td></td>
<td>B. Proportion of patients with HNSCC who had surgery, who have their pTNM stage reported to the BCR</td>
<td>78.4</td>
<td>95</td>
</tr>
<tr>
<td>DS-4</td>
<td>Proportion of patients with HNSCC who underwent FDG-PET(CT) before start of treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A. Stage I-II</td>
<td>22.9 ≤ 5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>B. Stage III-IV</td>
<td>47.6 ≥ 90</td>
<td></td>
</tr>
<tr>
<td>T-1</td>
<td>Proportion of patients with early stage (cI or cII) HNSCC who were treated with a single-modality approach</td>
<td>78.1</td>
<td>80-85</td>
</tr>
<tr>
<td>SX-1</td>
<td>Proportion of patients with non-metastatic T4a laryngeal cancer who underwent total laryngectomy</td>
<td>62.9</td>
<td>≥ 80</td>
</tr>
<tr>
<td>RT-1</td>
<td>Proportion of patients with HNSCC who were treated with postoperative radiotherapy in whom the radiotherapy was completed within thirteen weeks after surgery</td>
<td>48.5</td>
<td>≥ 90</td>
</tr>
<tr>
<td>RT-2</td>
<td>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 (except for patients with T4a laryngeal cancer)</td>
<td>≤ 70 years²; 58.2 ≤ 70 years²; 75-80</td>
<td></td>
</tr>
<tr>
<td>LN-1</td>
<td>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</td>
<td>32.7</td>
<td>80</td>
</tr>
<tr>
<td>LN-2</td>
<td>Proportion of surgically treated patients with HNSCC and cN0M0/x with any T stage (except T1 glottic cancer), who underwent elective neck dissection</td>
<td>56.4</td>
<td>≥ 90</td>
</tr>
<tr>
<td>G-1</td>
<td>Proportion of patients with HNSCC who die within 30 days of treatment with curative intent</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>A. Post-operative mortality</td>
<td>2.2 (1.7, 2.6)</td>
<td>&lt; 5</td>
</tr>
<tr>
<td></td>
<td>B. Post-radiotherapy mortality</td>
<td>4.0 (3.5, 4.6)</td>
<td>&lt; 5</td>
</tr>
<tr>
<td>ID</td>
<td>Quality Indicator</td>
<td>Result (%, 95% CI)</td>
<td>Target (%)</td>
</tr>
<tr>
<td>-----</td>
<td>--------------------------------------------------------</td>
<td>--------------------</td>
<td>------------</td>
</tr>
<tr>
<td>G-2</td>
<td>Observed survival 5 years after diagnosis (all HNSCC)</td>
<td>49.2 (48.2, 50.3)</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Oral Cavity</td>
<td>50.1 (48.2, 52.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oropharynx</td>
<td>44.7 (42.8, 46.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypopharynx</td>
<td>30.7 (27.9, 33.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Larynx</td>
<td>60.6 (58.7, 62.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Relative survival 5 years after diagnosis (all HNSCC)</td>
<td>55.0 (53.9, 56.2)</td>
<td>--</td>
</tr>
<tr>
<td></td>
<td>Oral Cavity</td>
<td>55.8 (53.7, 58.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Oropharynx</td>
<td>48.9 (46.9, 51.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Hypopharynx</td>
<td>33.7 (30.7, 36.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Larynx</td>
<td>69.5 (67.3, 71.7)</td>
<td></td>
</tr>
</tbody>
</table>

"For older patients no target was specified.
Source: BCR – IMA

3.4.1. Diagnosis and staging

Accurate diagnosis, staging and assessment of the condition of the patient are crucial to ensure appropriate treatment is delivered to patients with malignancies. Equally, timely treatment is essential, not only to increase the chance for cure, but also to alleviate the symptoms as soon as possible.

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 (Table 3, DS-1). As expected, the median delay to start primary radiotherapy was longer than for surgery (36 days vs. 24 days, respectively). Patients who received their first treatment in the centre where the biopsy was taken, were treated within a shorter timeframe than patients who were referred to another centre for treatment (median interval: 26 vs. 37 days, respectively).

There was a high variability between centres, particularly for centres that treated ≤ 200 patients during the six year period (Figure 2). Although the results compared favourably with those reported in other European countries (see Scientific Report, section 5.1.1), inspiration for a further improvement in this field can (among others) be obtained in Denmark, where organisational reforms coupled with the implementation of a fast track program resulted in significant reductions of waiting times between diagnosis and treatment, for both surgery and radiotherapy. 24
The proportion of HNSCC patients who were\textbf{ staged with MRI and/or CT before the start of the first treatment}, was 82.5%, which is below the target of 90%. A moderate variability between centres was observed, with many centres above and below the prediction intervals (Table 3, DS-2). 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 a MRI, irrespective of the anatomic site.

Precise specification of\textbf{ clinical and pathological stage} is an essential step in the clinical cancer pathway as it helps in planning the treatment or the renouncement of treatment (so that under- or overtreatment can be avoided), but it aids as much in predicting the patient’s prognosis. In addition, from the perspective of quality of care assessment, TNM stage information is also required for adequate case-mix adjustment of outcomes. But also, patients with unknown TNM stage cannot be included in the analysis of those indicators dedicated to specific subgroups of patients (e.g. SX-1 restricted to T4a laryngeal SCC). Because this underreporting of TNM stage information may bias the results, those centres which reported for less than 50% of their assigned patients stage information to the BCR, were presented differently (i.e. by an open triangle) in the funnel plots (e.g. Figure 2 and Figure 4).
For clinical (80.5%) as well as pathological (78.4%) TNM reporting, the results were far below the set target (95%; Table 3, DS-3). In several centres the reporting rate did not reach 50% (Figure 3). Although it cannot be disentangled whether the low reporting rates reflect an actual lack of correct and complete staging of individual patients or whether they are due to a flawed reporting process to the BCR, it is clear that in this area there is ample room for improvement.

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.7, 8 In 22.9% of clinical stage I-II HNSCC patients who underwent any kind of treatment, a whole-body FDG-PET(CT) was performed, which is largely above the target of 5% and thus unnecessary (Table 3, DS-4; Figure 4). On the other hand, in only 47.6% of clinical stage III-IV HNSCC patients who underwent non-palliative treatment, a whole-body FDG-PET(CT) was recorded, which is far below the target set at ≥ 90%. Even though some organizational (availability) and reimbursement issues at the time of the study may in part explain the low use of FDG-PET(CT) in patients with advanced stage disease, the results illustrate that more efforts are needed in this field so that the right group of patients benefits from this diagnostic tool but equally that the needless use of irradiation and costly equipment can be avoided.
3.4.2. Treatment

Whenever possible, guideline-concordant treatment should be offered, yet taking into account the patient’s condition and preferences.

In patients with early stage (cI or cII) HNSCC, a single-modality treatment is preferred in order to maximize organ functioning and minimize long-term side effects. This approach was offered to 78.1% of intended patients which is close to the set target (i.e. 80-85%; Table 3, T-1). Several hypotheses for these results were suggested by the clinical experts; for more details the reader is referred to the Scientific Report, section 5.2.1. Considerable differences were observed between the different anatomic sites (between 59.6% for hypopharyngeal SCC and 90.0% for laryngeal SCC).

According to the KCE guideline, total laryngectomy should be considered in patients with non-metastatic T4a laryngeal cancer. In our database, only 116 of these patients were identified; 73 of them (62.9%) underwent a total laryngectomy, which is below the set target (i.e. ≥80%; Table 3 SX-1). Yet, it is important to call attention to the fact that as many as 212 patients could not be included in the analyses since their TNM staging information was not specific enough, i.e. only T4 was reported to the BCR, without any further specification whether it was T4a or T4b. As mentioned before, this underreporting may have biased the results.

Several guidelines stress that postoperative radiotherapy should be started within 6 weeks after surgery and completed within 11-13 weeks after surgery in order to obtain a better outcome. Yet, in the present study only 34.1% of HNSCC patients initiated their postoperative treatment within 6 weeks and only 48.5% of HNSCC patients ended their radiotherapy within 13 weeks after surgery (Table 3, RT-1). From the scatterplots it can be deduced that the median end date of postoperative radiotherapy is nearly within the intended 11-13 weeks (i.e. 77-91 days) for all anatomic sites, yet in many centres the median is far above this time frame while in some centres the median is below 77 days (Figure 5). Substandard results were also reported for the UK and USA.

Concomitant platinum-based chemotherapy was offered to only 58.2% of patients younger than 70 years with locally-advanced stage (stage III and IVa-b) non-metastatic HNSCC who had radiotherapy, which is far below the target set by the clinical experts for that patient group (i.e. 75-80%; Table 3, RT-2). Variability between centres was moderate. An additional 7% of this patient group received concurrent Cetuximab. In addition, 29.2% and 20.5% of patients with stage III and IV non-metastatic oral cavity and oropharyngeal SCC was offered induction chemotherapy followed by RT which is not according to the guidelines. This approach is only an acceptable therapeutic option for larynx preservation in advanced laryngeal and hypopharyngeal SCC. However, It has to be mentioned that it is very well possible that the number of patients who received induction chemotherapy has been overestimated (due to invoice issues, see Scientific Report, section 5.2.4) and that in reality some of these patients were treated with concomitant CRT.

The proportion of patients with node-positive HNSCC in whom according to the KCE guideline 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, was only 32.7% (Table 3, LN-1). A positive signal is that this proportion increased during the study period (from 27.7% in 2009-2011 to 37.1% in 2012-2014).

Among HNSCC patients who were staged as cN0M0/x and who had surgery with curative intent, only 56.4% underwent an elective neck dissection (Table 3, LN-2), which is much lower than the target set at ≥ 90%. An additional 12.8% received adjuvant RT while for 30.7% of this patient group no neck treatment was identified in the database. Several hypotheses for this inferior result were suggested by the clinical experts (for more details the reader is referred to the Scientific Report, section 5.2.6).
Figure 5 – Time from date of surgery (with curative intent) to the end date of adjuvant radiotherapy, by main treatment centre (2009-2014)

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
3.4.3. Safety of care – 30-day mortality after treatment with curative intent

Safety of care delivered to patients who received treatment with curative intent, was analysed separately for patients who had surgery and for those who had radiotherapy as main treatment. For both treatment groups, the results were good: 30-day mortality was 2.2% and 4.0% for surgery and radiotherapy, respectively (Table 3, G-1). They are in line with results reported from other countries (UK and USA). Variability between centres was not only assessed with funnel plots (see Scientific Report, section 5.3), but in order to take differences in patient case-mix between centres into account, adjusted Odds Ratios per centre were calculated (Figure 6). Some variability in the risk of 30-day postoperative mortality among the surgical centres (Figure 6A) as well as the RT centres (Figure 6B) was observed. But, as the confidence intervals of nearly all centres crossed value 1, most centres do present a postoperative mortality rate which is not significantly different from the overall rate. However, what is more important: for 60 out of 96 surgical centres and 2 out of 26 RT centres the adjusted 30-day mortality could not be calculated as their volume was too small. These centres treated less than 30 patients over the six year study period, or less than 5 patients a year. Hence, Figure 6 does not tell us anything about the mortality in these very low-volume hospitals.
Figure 6 – Adjusted* Odds Ratios for A. 30-day post-operative mortality by surgical centre and B. 30-day post-radiotherapy mortality by RT centre (2009-2014)

* 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; in the forest plots, 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.

Note to A: 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. Note to B: 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.

Source: BCR – IMA
3.4.4. Survival after the diagnosis of HNSCC

Overall, the observed survival was 77% at 1 year and decreased to about 50% at 5 years (Table 3, G-2). The highest survival probability was observed among patients with laryngeal SCC and the lowest in patients with hypopharyngeal SCC, which 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. The relative survival (78.2% and 55.0%, at 1 and 5 years, respectively) was comparable to the observed survival, pointing out that in this population the probability to die is mainly attributable to the HNSCC (Table 3). 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 EUROCARE-5 study assessed cancer survival in (among others) 250,000 head and neck cancer cases (nasal cavities, thyroid and salivary glands excluded) from 86 cancer registries. Belgian results – indeed limited to data for Flanders – for the incidence years 2000-2007 were good in terms of age-standardised 1-year relative survival (75.8% compared to a mean for Central Europe (i.e. Austria, Belgium, France, Germany, Switzerland and the Netherlands) of 75.9%), but below average for age-standardised 5-year relative survival (46.2% compared to a mean for Central Europe of 48.6%). In a Dutch study with 2,094 HNSCC patients diagnosed in 2008, the 5-year observed survival was for all four anatomic sites more favourable. Yet, the differences between the Netherlands and Belgium in terms of 5-year relative survival were less pronounced in another Dutch study, reporting on patients diagnosed with HNSCC between 2007 and 2011. For more details the reader is referred to the Scientific Report, section 5.4.

3.5. Association between hospital volume and survival

Given the large dispersion of care for HNSCC patients in Belgium, we could not pass over the evaluation of the impact of hospital volume on outcome without comment. HNSCC patients who were treated in high-volume centres (> 20 patients/year) had a statistically significantly higher chance to survive than their peers who were treated in low-volume centres (≤ 20 patients/year) (Table 4).

Table 4 – 1-, 2-, and 5-year unadjusted observed and median survival for all HNSCC, by main treatment volume (2009-2014)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>N centres</th>
<th>N patients</th>
<th>HR (95% CI)*</th>
<th>1-year (%)</th>
<th>2-year (%)</th>
<th>5-year (%)</th>
<th>Median observed survival (years)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>99</td>
<td>9,175</td>
<td>0.991 (0.995, 0.998)</td>
<td>76.7 (75.8, 77.5)</td>
<td>65.1 (64.1, 66.0)</td>
<td>49.3 (48.3, 50.4)</td>
<td>4.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Main treatment volume*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤ 20 patients per year</td>
<td>76</td>
<td>2,135</td>
<td>0.996 (0.995, 0.998)</td>
<td>70.0 (68.0, 71.9)</td>
<td>60.2 (58.1, 62.2)</td>
<td>46.3 (44.1, 48.5)</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td>&gt; 20 patients per year</td>
<td>23</td>
<td>7,040</td>
<td>1.000 (1.000, 1.001)</td>
<td>78.7 (77.7, 79.6)</td>
<td>66.6 (65.4, 67.7)</td>
<td>50.2 (49.0, 51.5)</td>
<td>5.1</td>
<td></td>
</tr>
</tbody>
</table>

* 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.

Source: BCR – IMA
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, the hazard to die of any cause decreased on average with 0.4% per increase of one additionally treated patient. As is displayed in Figure 7, once the number of assigned patients was higher than 20 patients a year, there was no further decrease in hazard to die. Over the six year study period, 76 centres treated 20 or even less HNSCC patients per year, while 23 centres could be considered high-volume centres. Here it is further illustrated that patients treated in high-volume centres had significantly higher chances to survive than their peers.

Figure 7 – Predicted Hazard Ratio to die according to main treatment volume over the 2009-2014 study period

These results are supported by similar observations from several countries: high-volume hospitals are predictors of better overall survival for head and neck cancer patients.32, 34-36 Several hypotheses explaining this volume-outcome association have been suggested in the international literature; they are further elaborated in the Scientific Report, section 5.5.

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’.37,38 The authors recommended to concentrate the care for patients with head and neck cancer care in reference centres, where a multidisciplinary team of experts (among others pathology, radiology, nuclear medicine, head & neck surgery, radiation oncology, medical oncology) dedicated to head & neck cancer typically manage a large number of patients per year.

Additional volume-outcome analyses were performed assessing the association between surgical volume and observed survival on the one hand and radiotherapy volume and observed survival on the other hand. No statistically significant associations were observed, which may (in part) be explained by the large dispersion of care, resulting in many centres with low-volumes. Likewise, no statistically significant associations were recorded between surgical volume and radiotherapy volume and 30-day mortality, not surprising given the small cells but also the small number of ‘events’ (i.e. deaths).

Last but not least, when interpreting the data, it is important to realise that some of the centres that are categorised as high-volume centres are in reality only a cluster of recently merged low-volume centres. These merged centres may still act and manage patient care as individual (small) entities without centralising some care aspects (e.g. diagnosis and management of rare cancers), with each low-volume centre still taking care of a small number of patients. Patients cared for 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 these centres. Yet, it can be hypothesized that if several high-volume centres are in reality still working as clusters of small entities, this may have attenuated the differences in survival probabilities between high and low-volume centres and this may (in part) explain why the additional volume-outcome analyses at the level of surgery and RT centre did not reveal significant results.
4. 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. 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 3.4.2) are not included in the database, while they may explain (in part) why certain predefined 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 from various horizons with regards to specialty, with profound experience in the diagnosis and treatment of patients with head and neck cancers. They work in academic and non-academic centres, geographically spread over the country and know the Belgian context (e.g. fees, reimbursement rules) very well. 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 2.2, 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: 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.41

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).42 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.43

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.44 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 financing of the MDT discussion and the data managers is linked with the quality of data reporting to the BCR?

5. 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.9

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’, 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.

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 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. 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.

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

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 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.

\[\text{f} \quad \text{The KCE has sole responsibility for the recommendations.}\]
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:
  - P16/HPV status for oropharyngeal cancers
  - Type of surgical procedure (incl. purpose of procedure: diagnosis vs. treatment), organ and/or function sparing treatment
  - Radiotherapy schedule (e.g. fractionation scheme, start and end date)
  - 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 radiology and 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.


34 Quality indicators for the management of HNSCC KCE Report 305Cs


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