Quality indicators in head and neck oncology

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CHAPTER 1

General introduction and outline of thesis

GENERAL INTRODUCTION

Head and neck cancer

Head and Neck cancer represents a heterogeneous group of tumors. The majority of these lesions arises from the mucosa of the upper aerodigestive tract and is classified as squamous cell carcinomas. Other, rarer entities are adenocarcinomas or sarcomas. Classical risk factors for the development of mucosal head and neck squamous cell cancer are smoking, alcohol consumption or the combination of both[1]. The last decades the HPV-16 was added as an important etiologic factor mostly affecting younger patients[2]. Nasopharyngeal carcinoma, except for squamous cell carcinoma, forms an exception to the above-mentioned etiologies and is strongly related to Epstein Barr virus, but genetic factors and environmental influences are also of importance in the pathogenesis of this disease. Much less is known about the etiology of salivary gland cancer. Exposure to radiation in the past is suggested as risk factor, based upon studies of atomic bomb survivors from Japan[3] and patients irradiated in their childhood for any cause[4,5].

For initial treatment, surgery was long considered the only curative treatment option for most head and neck carcinomas. Since this treatment modality causes serious functional deficits in locally advanced cases, the combination of chemotherapy and radiotherapy gained terrain rapidly as organ sparing therapy during the last decades[6]. Next to chemoradiotherapy, radio-sensitizing drugs (like the monoclonal antibody cetuximab) were introduced in order to improve outcome[7]. The radiation component of these multimodality treatments has improved over the last decade. The introduction of intensity modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT) have led to an improvement of efficacy and also decreased toxicity (i.e. xerostomia) of radiotherapy, compared to the previously used 3D conformal technique[8,9]. Surgical techniques also evolved during the last decades, with the introduction of minimal invasive techniques, such as CO2 laser[10] and transoral robotic surgery[11] for small, localized cancers in the oral cavity, larynx and pharynx. The anatomically complex head and neck area makes treatment of head and neck cancer challenging, particularly since there is a delicate balance between functional and oncologic outcome. The influence of inter-patient variety and treatment choices on this balance makes that the field of head and neck cancer can be classified as “high-risk” cancer care.

Concept of quality

In general, quality of an ordinary product is defined by the phrase: "It does what you expect of it to do". This might be a realistic expectation for simple products, but defining "quality" in healthcare is much more complex for multiple reasons. The Institute of Medicine[12], a division of the National Academies of Science, Engineering and Medicine in the USA, issued the following definition for quality of care: "Quality of care is the degree to which health services for individuals and populations increase the likelihood of desired health outcomes and are consistent with current professional knowledge"[12]. It helps government and patients by providing information to make proper health decisions and by providing robust evidence with help of experts in the field. Another, more detailed definition, also issued by the same institute is: "Getting the right care, to the right patient, in the right setting, in the right way, by the right (team of) doctors, at the right time, every time!"
Within quality of care several quality domains can be defined[13]:

Safety	Health care is intended to help patients, so adverse events must be avoided at any time.
Effectiveness	Use the available health care wisely, according to up to date scientific data. In short: avoid over- and underuse of the available health care facilities.
Patient-centered	Health care should be provided in a tailored fashion to individual patients with respect to all patients' with their preferences, needs and values.
Timeliness	Finding the optimal balance between available health care facilities and reducing (harmful) delay.
Efficiency	In this era of increased interest in durability, also health care providers must minimize waste of products, but also minimize waste of time, ideas and energy.
Equity	It must be unthinkable that quality of provided care is based on ethnicity, gender, geographic location and socio-economic status.

In order to critically evaluate quality of care, the perspective needs to be clear. Each time one has to question whether it concerns the health care system as a whole, a single health care institution, a single health care professional or a specific intervention[14,15]. After assuring the domain focus and the approach, the next step concerns the evaluation of the actual quality. In this thesis our focus is on the domains: safety and effectiveness.

Quality assessment

In 1988, Donabedian et al.[15] suggested the implementation of an indicator model, based upon three types: structure, process and outcome indicators. All three are separately involved in assessment of quality, but are also causally cross-linked. Nevertheless, by exploring these three separately, it is possible to gain better insight in the complexity of health care quality assessment. The following issues have to be addressed before assessing quality: Who is being assessed? What are the activities being assessed? How are these activities supposed to be conducted? What are they meant to accomplish?
After analyzing these issues, the context of the system being assessed might become more evident.

I. Structure indicators

Structure indicators describe the health care environment, the setting in which care is provided. Examples in this group are the number of qualified personnel and the equipment of the assessed facility. Structure indicators are meaningful for explanation of results of exceptional surgeries like pancreaticoduodenectomies [16], esophagectomies[17], cystectomies[18] and other high risk surgeries like open cardiac surgery[19]. The use of structural indicators often has the advantage of easy and inexpensive access to data, mostly administrative of origin. The biggest disadvantage of using these indicators is that they are only proxies for quality of care and no guarantee for it. Moreover, structural indicators lack the opportunity to learn from differences in care processes. The consequence of using structural indicators is that clinical improvements are obtained more slowly or even impossible: low volume hospitals cannot turn into high volume hospitals at once.

II. Process indicators

Process indicators describe the process of health care using organizational parameters involved in the primary care process. This involves the whole diagnostic and, medical decision-making process as well as the treatment trajectory. Often-discussed examples of process indicators are waiting times, discussion in a multidisciplinary team (MDT) and pre-operative antibiotics. Process indicators are mostly based on evidence-based guidelines or consensus-based quality standards, and measure the adherence to these guidelines or standards on a patient level. An often-used example of a process indicator is waiting time. The shorter-the better is the adagio for waiting times, but is it gut feeling or evidence based?

Another example of a process indicator is the routing of surgical specimen after resection, i.e. the way histopathology is acquired and reported.
As mentioned above, evidence based guidelines are often the foundation for process indicators, which measure the implementation of these guidelines in real clinical practice (locally or nationally). Examples of these are diagnostic trajectory guidelines and definition of optimal treatment regimes. For instance, magnetic resonance imaging (MRI) has superior soft tissue contrast that is crucial for delineating tumor extension in the head and neck area. However, MRI has its limitations in moving target volumes, i.e. the larynx during swallowing reflexes, thus for imaging of the laryngeal area a more rapid imaging technique, computer tomography (CT), is preferred. This illustrates the basis of a process indicator evaluating the use of the right diagnostic modality for the right tumor extension.
Many process indicators are based on what is considered strongly evidence based, i.e. based on results from randomized trials or meta-analyses. New scientific evidence can change 'state of the art' care processes within short time periods. Striking examples of randomized trials in the head and neck cancer treatment leading to paradigm shifts are: the Veterans Affairs Administration[20] and RTOG[21] organ preservation trials in laryngeal cancer with platinum-based chemo-radiotherapy. The RADPLAT trial[22], showing the non- inferiority of intravenous administration of Cisplatin compared with intra-arterial delivery of Cisplatin and the Bonner trial[7] combining Cetuximab and radiation for organ preservation with less toxicity. These studies have led to alterations in guidelines.
Although working according to guidelines can be seen as useful process indicator, there remain some pitfalls. For instance: trial populations may differ substantially from the population of patients seen in daily practice, which may hamper the one-on-one transfer of (positive) trial results. Or what used to be state of the art care can change over time, causing the process indicator outdated, especially if a guideline is not changed quickly enough. For example: the above-mentioned RTOG91-11[21] became the standard for larynx preserving therapy in a very short time frame, although the pendulum now seems to swing back in favor for surgical treatment[23].
Process indicators have proven to be of general importance since the 20th century. However, they also carry possible disadvantages like the easy influences of population mismatches. A currently discussed topic in head and neck cancer societies, in line with population mismatch, is whether all data on oropharyngeal cancer also count for HPV positive tumors[24], because over the years they have constituted a distinct entity[25]. General process indicators developed for oropharyngeal cancer might fall short in the current practice where there is a dichotomy in oropharynx cancer based on HPV status. Reason for this shortcoming is that increasing evidence appears about differences in, for instance chemo- and radiotherapy sensitivity between HPV positive and HPV negative oropharyngeal cancers[26].

Currently a multicenter prospective randomized trial (NCT01687413) is accruing patients to determine whether treatment de-intensification is safe in HPV positive oropharyngeal cancer patients. This data can be used to define HPV positive/negative specific process indicators.
Moreover, despite the availability of a validated guideline, in the era of shared decision-making, sometimes patients choose for personal reasons to be treated differently than the guideline prescribes. Therefore, process indicators should not pursue 100 percent guideline adherence, because real world clinical practice differs from the trials the guidelines were based on. These two examples show clearly the difficulty in defining evidence based process indicators. This stresses the need for choosing carefully relevant indicators and to update them regularly.

III. Outcome indicators

The third component of Donabedians paradigm consists of outcome indicators, which denote the actual outcome of health care, provided, tailored to the health of individual patients or populations. The final outcome is what counts most for individual patients and doctors. From an economical point of view, health insurance companies are interested in outcome as well, because this helps them to decide which hospital to contract for a specific care product. The involved parameters cover a broad spectrum ranging from very objective (death) to more subjective [questionnaires, like patient reported outcome (PROM) and experience (PREM) measures]. This spectrum contains on the one hand pearls, for example the opportunity to inform patients on outcome for their specific disease, but on the other hand also pitfalls when an outcome measure does not match with the clinical significance. For example, overall survival is not always a meaningful outcome parameter in palliative care, while it is meaningful in curative care. So when interpreting outcome parameters one needs to know the context in which they were measured and investigated. Another aspect of outcome indicators is that outcome is often determined by a combination of factors instead of by one specific factor. This makes it difficult to design effective measures to improve outcome. Interpreting differences in indicators and thus assessment of quality of care is only possible by knowing the cross-linked connection between the three types of indicators.
An example to illustrate the complexity of assessment of quality of care delivered by individual providers can be illustrated for laryngectomies performed in different institutes:

Structure:

- o Are these laryngectomies performed in a certified head and neck cancer center?
- o What is the procedural volume of laryngectomies in this specific center?

Process:

- o Are all pharyngeal defects primary closed?
- o How is the closure procedure conducted?
- o Is oral intake resumed immediately post-surgery[27]?
- oAre patients discussed in a MDT meeting?

Outcome:

- o What is the complete resection rate?
- o How many patients have had complications postoperatively and how many die due to these complications (failure to rescue)?
- o How is the quality of life?

To make valid comparisons in quality of care between centers performing laryngectomies, risk-adjustment of outcome indicators must be appropriate and could be focused on the unraveling of differences between centers with attention for:

- o Percentage of patients with multiple comorbidities
- o Percentage of smokers
- o Percentage of locally advanced tumors
- o Percentage of primary tumors vs. recurrences
- o Percentage of patients with prior treatment with radiotherapy

The connection between the different indicators can be illustrated by the following hypothetical example: a certain hospital has the opportunity to appoint an additional, certified head and neck specialist (structure indicator – number of certified specialists). Due to this extra physician the outpatient clinic capacity increases and waiting times for patients shorten (process indicator – time between first visit and treatment). Also, the volume of the hospital can be increased (in case the number of patients is unlimited). Previously, the organization of a MDT meeting was not possible due to an under-staffed department, but now regular MDT meetings can be organized (process indicator – number of patients discussed in a MDT). This might lead to improved treatment strategies reflected in higher complete resection rates, better survival and quality of life (outcome parameters).

However, it remains still unclear which parameter is crucial for the improved outcome of the individual patient: it could be the experience of the surgeon, the MDT discussion, or the shorter waiting time or a combination of these factors.
The quality of care concept of Donabedian et al[15] is a tool to clearly describe and organize quality of care. The two components (structure, process) are complementary to each other and all components are necessary to describe quality as complete as possible [figure 1].

Quality improvement

Randomized controlled trials

Striving for the best result for the individual patient is an inherent trait of health care professionals. One of the tools to achieve better clinical results is by conducting Randomized Controlled Trials (RCT). Pubmed generates almost 400,000 hits for RCTs from 1970 to 2015. Half of these RCTs are published during the last ten years, indicating the increased interest in health care improvement. Whether this flood of data leads to optimal quality of care for every patient remains questionable. Quality or impact of a single RCT (as can be assessed by the critical appraisal tool for RCT (Oxford university 2005 ©) can be too limited to initiate changes in nationwide guidelines (strict inclusion criteria or inappropriate primary outcome). However, it can provide useful information for the treatment of specific subgroups of patients. Moreover, limited impact RCTs can be included in meta-analyses contributing to highly powered evidence. Not all clinical questions regarding clinical problems in individual cases can be solved by RCTs. To search for epidemiological trends or to investigate outcome from one institute, population-based or cohort studies can be more suitable and can provide 'real world' clinical evidence for smaller patient groups.

Quality standards

Next to all research efforts, several other strategies are internationally used to improve quality of care, for instance: regulation of care, marketplace competition, payment incentives, or the introduction of a program for continuous improvement of quality (which is encouraged by organizations like The Joint Commission on Accreditation of Healthcare Organization, the National Committee for Quality Assurance)[28] or in the Netherlands "Quality institute" as part of "The national health care institute".
The most relevant factor for the Dutch situation is regulation of care and can be determined by setting minimal volume standards. The Dutch Federation of Oncologic Societies (SONCOS) was founded in 2009 with the objective to improve collaboration between three oncology-oriented specialisms (surgical oncology, medical oncology and radiation oncology). One of the achievements of SONCOS is a structured document with multidisciplinary quality standards for oncologic care in general and for each tumor type.

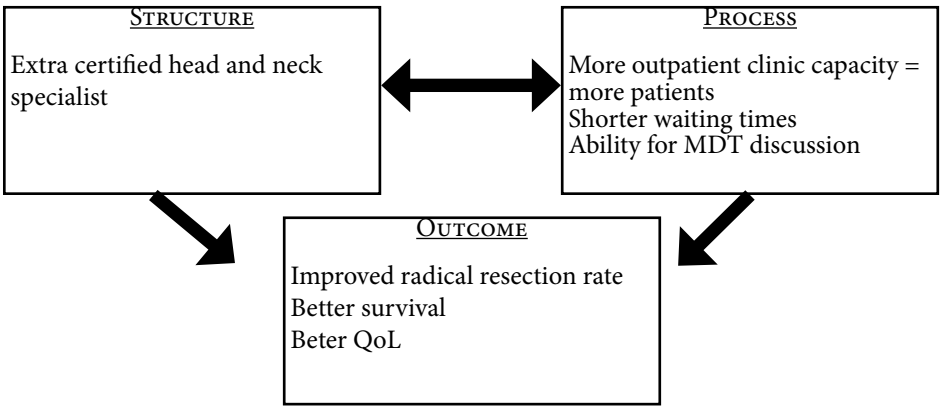

Figure 1 Example of the relation between quality indicators. This example starts with an extra certified head and neck specialist. Due to extra capacity, shorter waiting times and increased patient volume could be reached. This creates higher efficiency and leads to improved oncologic outcome and patient quality of life (or another patient reported outcome) with two components (structure and, process) acting in a complementary fashion.

Today, more than 20 professional societies contribute to this document and most stakeholders, like the Health Care Inspectorate (IGZ), health care Insurance companies, hospitals and policy makers have adopted the SONCOS quality standards. Cancer or procedure specific volume standards are an important part of the document and are the only standards that can be actively enforced by insurers and inspectorate.

Volume

Luft et al.[29] were the first to publish on volume-outcome relationship as quality indicator in surgery. In their paper they questioned whether higher hospital volume leads to lower mortality[29]. In total 1498 hospitals were included and 12 procedures of varying complexity were examined. In a multiple regression model, including hospital size, teaching status, geographical location and cost improvement, volume was one of the most important factors determining mortality. The authors concluded that experience and health care infrastructure were the main explanations for this finding in high-risk surgery.

Many studies[16,17,30-34] have shown beneficial outcome for high volume hospitals, using mortality and/or survival as outcome. Soon it became clear that this relationship was most clear in high-risk procedures like pancreaticoduodenectomies (i.e. Whipple procedure), esophagectomies, gastrectomies, cystectomies and radical prostatectomies (table 1)[16,17,30-32].

Table 1. A sample from the literature on volume-outcome relationship in oncological procedures.					
Author	Year	N=	Procedure	Outcome	Volume effect
Van Heek[17]	2005	19688*	Pancreaticoduodenectomy	Mortality	Hospital volume: inverse relation
Wouters[18]	2012	80202*	Esophagectomy	Mortality	Hospital volume: inverse relation
Wilt[31]	2008	206141*	Radical prostatectomy	Mortality	Hospital volume: inverse relation
Van Gijn[35]	2010	80481*	Colorectal	Mortality	Hospital volume: inverse relation
Dikken[30]	2013	n.r.*	Gastrectomy	Mortality	Hospital volume: inverse relation
Hollenbeck[32]	2007	4465*	Cystectomy	Mortality	Hospital volume: inverse relation
Abbreviations: n.r. not reported, * Systematic reviews					

In conclusion, although volume as quality indicator is determined by multiple parameters, currently available data repeatedly show that higher hospital volume leads to better outcome in different types of high-risk surgery[16,18,34,36,37]. Therefore, centralization of services for high-risk or complex cancer treatment could lead to quality improvement and better outcomes. Pieper et al.[34] evaluated 5 systematic reviews on the volume-outcome relationship for clinical outcome (postoperative mortality, complications and survival) in surgery. Fourteen types of surgery, including benign as well as malignant diseases, were included. Besides the positive volume- outcome relationship, the authors defined some methodological pitfalls. The first is the definition of high volume hospitals: numerically high volume hospitals in the Netherlands for example could be defined as low volume in the United States, indicating that the definition of high volume hospitals is partly geographically determined. For a proper judgment of volume effects, correction for case-mix is indisputable, although it remains impossible to correct for every single variable of case-mix. This renders volume to be a surrogate indicator for several unknown factors. For example, a high volume hospital with a well-functioning tumor board, might lead to excellent patients' outcomes, while the actual interaction of the tumor board remains an undetectable factor.

Clinical Audit

Next to regulation of care by setting volume standards, programs for continuous improvement of quality are important. Registration programs play a pivotal role in this respect. In the Netherlands, registries like: "The nationwide network and registry of histo- and cytopathology in the Netherlands" [PALGA] and the Netherlands Cancer Registry (NCR) were founded in the eighties. This NCR covers all newly diagnosed cancers by registering all pathology reports and hospital discharge diagnoses.

Specifically trained data managers gather several patient, tumor and treatment parameters in the individual hospitals. Vital status is annually assessed by linkage to Municipal Personal Records (in Dutch: "Basisregistratie Personen or BRP"). Over the years, the nation-wide coverage reached at least 95%[38]. This registry is a unique base for epidemiological studies and due to its high coverage it is also suitable for quality control studies.
Individual hospitals have been scoring complications for decades, but since 2000 better-organized registries started evaluating the whole process of hospital care and its outcome, adjusting for differences in case-mix between participating hospitals. An example are the 23 quality registries of the Dutch Institute for Clinical Auditing (DICA)[39], which was founded in 2010 after the successful initiation of the Dutch Surgical Colorectal Audit in the Netherlands. Initially, the DSCA was a surgery-based registry, which started with the registration of primary colorectal cancer patients' characteristics, treatment and outcome. Feedback is given continuously through a web-based system in which hospitals find their own results in perspective to the other hospitals in the country (benchmarking). This is called the audit-feedback principle and leads to an awareness of each hospital's performance in comparison to the rest of the hospitals. In case hospitals persistently perform below the national average, this system will give a notice. A team of specialists appointed by the Association of Surgeons in the Netherlands will visit such a hospital to try to identify points for improvement, resulting in a thorough problem analysis and quality improvement program. Subsequently the continuous audit monitors the effect of the initiated quality improvement programs, which completes the "audit-cycle".

Head and neck cancer and quality

The head and neck departments in the Netherlands have been pioneers in centralizing multidisciplinary care in order to improve quality. Already in 1984 the Dutch Head and Neck collaborative group was founded[40]. Goals were initially to share knowledge and collaborate in research, but soon after foundation quality improvement was added by stating that every single malignant head and neck tumor should be treated in one of the eight head and neck cancer centers or one of the preferred partners. This resulted in a centralization rate of above 95% in the mid 90's[41]. The remaining 5% possibly were small T1 laryngeal tumors that were easily removed by the oto-rhinolaryngologist or salivary gland carcinomas that were thought to be benign on preoperative workup. Nowadays, six preferred partner hospitals are participating in the Netherlands head and neck oncology center network, resulting into 14 certified head and neck centers in the country.
Head and neck cancer patients often deal with swallowing problems and impaired speech either induced by tumor growth or by treatment, with serious consequences for their quality of life.

Since both function and esthetics are easily affected, treatment of head and neck cancer is typically dependent on a multidisciplinary approach, in which the surgeon (oncologic and reconstructive), radiation oncologist, medical oncologist and paramedics play their individual roles.

An integrated multidisciplinary care program, containing all disciplines, has led to increased patients satisfaction and higher quality of life[42]. Such a quality improvement program is made up by different indicators, which cover all three fields of quality (structure, process and outcome). Ouwens et al.[43] developed a set of clinical quality indicators consisting of eight specific integrated care indicators (for instance, availability of a clinical pathway, case managers and the number of patients that feel well informed) and 23 specific head and neck indicators (for instance, availability of head and neck radiologists, number of patients with swallowing problems and the availability of a multidisciplinary stop-smoking program)[43]. With this set of indicators, they studied head and neck cancer care quality in one certified Head and Neck Center. They found that especially assessment of nutrition, waiting times; swallowing and speech rehabilitation and emotional support leave room for improvement. All of these were patient-oriented items, showing the gap in focus between doctors and patients in relation to quality of care improvement. An implementation study of the program published by Ouwens et al.[44] also showed the positive effect of such integrated care program on quality of care in head and neck cancer patients, especially on patient information by introducing an information folder, waiting times by optimizing the process and improved nutrition guidance by strict dietician control (improvement from 44% to 88% in dietician visits). The multidisciplinary rehabilitation program after treatment for head and neck cancer is another example of an evidence based quality improvement program. This program contains a dedicated multidisciplinary (para-) medical team of specialists in rehabilitation aiming for a personalized rehabilitation program, which leads to improvement in health related quality of life and also in less distress[45].

The aforementioned audit-feedback principle, like the DICA system, has also been assessed for head and neck surgeons in MD Anderson, Houston Texas[46]. Investigators evaluated a patient cohort containing 2618 procedures (2004 – 2008). After evaluation several (quality) indicators they confronted the surgeons/departments with their individual performance. Thereafter, they evaluated a post feedback series of procedures (n=1389) from 2009-2010, to check the influence of feedback on performance. They found a significant decrease in the mean length of stay as well as the number of negative performance measures (mortality, readmission, reoperation, surgical site infection, blood transfusion).

This thesis deals with an exploration of potential indicators in a well-centralized head and neck cancer setting and is outlined as follows.

OUTLINE OF THE THESIS

Quality of health care is a very large and unbounded concept. In order to streamline this research project, the concept of quality assessment of Donabedian et al15 was used. This thesis describes quality of head and neck cancer care in the Netherlands. It is divided into the three components of quality indicators, which are structure, process and outcome.

STRUCTURE INDICATORS

Because head and neck cancer is centralized the Netherlands, the question arose whether increasing volume of hospitals improves outcome. In CHAPTER 2 a literature search was performed to find evidence whether higher (centralized) volume in head and neck is associated with better outcome.
In CHAPTER 3 variation of care was evaluated in seven head and neck cancer centers and three preferred partner hospitals to assess whether centralization leads to uniformity in diagnostic and treatment processes

PROCESS INDICATORS

In CHAPTER 4 we analyzed the influence of waiting times in the Netherlands Cancer Institute on survival as process indicator. Processing of pathological specimens is another important process indicator, which is almost unknown among clinicians. All of the steps involved in the pathology process are quality sensitive steps, meaning that small disturbances can lead to misinterpretation or even wrong diagnosis. To uniform these steps all pathology laboratories in the Netherlands work with quality assured protocols.
The influence of a pathology protocol change has been investigated in CHAPTER 5 with focus on lymph node yield in neck dissection specimens, comparing two examination protocols.
CHAPTER 6 focuses on the outcome variation evolving from the pathology protocol of lymph node dissections. In this chapter we studied the variation in prognostic value of Lymph Node Ratio (LNR) in relation to changes in pathology protocols.

OUTCOME INDICATORS

Outcome in cancer care is mostly defined as overall survival or disease specific survival. Besides the variation of care, CHAPTER 3 also describes different outcome indicators (survival and recurrence rate) for head and neck squamous cell carcinomas in the Netherlands.

This chapter specifically describes variables (including hospital volume) influencing the outcome of head and neck cancer patient cohort from 2008.
Despite the fact that salivary gland carcinoma treatment should be centralized in head and neck cancer centers; the centralization rate remains lower for salivary gland tumors compared to most other head and neck carcinomas. Salivary gland tumors are unique since this group consists of both benign and malignant neoplasms. To achieve better knowledge of the epidemiology of salivary gland carcinoma we performed nationwide studies on outcome of salivary gland carcinomas over the past 21 years (Chapter 7) and pleomorphic adenoma over the same period (chapter 8).

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