IMPROVING PERSONALIZED MEDICINE IN HEAD AND NECK ONCOLOGY

Shared Decision Making and Rehabilitation

A.N. Heirman

IMPROVING PERSONALIZED MEDICINE IN HEAD AND NECK ONCOLOGY:

'Shared Decision Making and Rehabilitation'

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Prologue

Prologue

This is the story of mr. T., a 66-year-old man. He is healthy, although he has a known high blood pressure for which he takes medication. He works as a janitor at a high school, but he is nearing retirement. In his free time, he enjoys being at home with his wife and dog, and playing cards at the community center. They have two daughters, and one grandson.

However, recent months have brought unwelcome health concerns. Persistent hoarseness and worsening coughing have disrupted his routine, making communication increasingly difficult as his voice weakens, impacting both his personal and professional life. Concurrently, he experiences discomfort in his throat, occasionally extending to his left ear. Initially, his general practitioner prescribed antibiotics, suspecting a throat or airway infection, but unfortunately, these provided no relief. Consequently, Mr. T. was referred to the ENT department, where a thorough examination uncovered concerning abnormalities in his vocal cords during an endoscopy procedure.

Recognizing the urgency of the situation, the ENT specialist promptly referred him to the Head and Neck Oncology department, where he was scheduled for evaluation the following day. During this evaluation, it was revealed that Mr. T. had been a heavy smoker since the age of 16, with unsuccessful attempts at quitting. Additionally, he regularly indulged in alcohol, consuming five cans of beer post-work and whiskey during Friday card games.

Following extensive evaluation, Mr. T. and his wife received devastating news from the doctor: laryngeal carcinoma, which had metastasized to his lymph nodes. After consultations with medical experts, it was determined that a total laryngectomy offered the best chance of survival. Radiation treatment was considered as an alternative, but with a significant risk of rendering his larynx nonfunctional, ultimately leading to the need for a total laryngectomy.

Back home, they feel overwhelmed and full of questions, after consultations with the head and neck surgeon, radiation oncologist, and oncologist. “What is metastasis anyway?” asks his wife. “And will you never be able to talk again?” “I think I can talk again, the doctor mentioned something about a voice prosthesis and a humidifier or something,” says Mr. T. “But what should I do? Everything sounds terrible. Am I going to die?”

Mr. T. and his wife are lost. Ultimately, they agree with the surgery since the doctor said it offers the best chance of survival for him.

The surgery is performed, and Mr. T. is hospitalized for 19 days. He hadn't expected it to be so hard. Pain, coupled with difficulty communicating through the voice prosthesis, fuels anxiety. Upon returning home, familiar surroundings offer little comfort as he navigates a changed existence.

Months later, tentative adjustment begins. Managing his stoma and communicating with the voice prosthesis gradually become routine. He has opted for early retirement. Initially, he mentioned dropping by occasionally, yet he does not dare to. Card games, once a source of enjoyment, are now abandoned. Participating in group conversations is hard, and how is he supposed to speak with a voice prosthesis while holding all his cards?

His life is far from what it once was. Every day, he doubts his decision. What if he had chosen radiation? Perhaps his larynx would have remained functional, sparing him the life-changing side effects of a laryngectomy. But then again, could life have taken a turn for the worse? Or would it have been better to have done nothing at all and faced the inevitable outcome of cancer? After all, he had enjoyed a great life.

Well, either way.. He needs to go to the hospital; his voice prosthesis is leaking. Again..

Chapter 1

General introduction

General introduction

The experience of patients with head and neck cancer (HNC), like Mr. T.'s story, begins a challenging journey. Initial encounters often involve consultations with a head-and-neck surgeon, a radiation oncologist, and occasionally, a medical oncologist and dentist. Additionally, patients will interface with various allied health professionals, including speech-language therapists (SLPs), dieticians, and head-and-neck oncology nurses. Given the aggressive nature of HNC, there exists a pressing sense of urgency. In the midst of numerous consultations with various specialists, patients face the heavy burden of their diagnosis and its emotional impact, while considering their treatment options, which could even include choosing not to undergo treatment at all.

In this thesis, we delve into the multifaceted landscape of HNC care, exploring the challenges faced by patients and healthcare professionals alike. Through an exploration of shared decision-making dynamics and rehabilitation strategies, we aim to contribute to a deeper understanding of HNC management. With this introduction, I will guide you through some key aspects crucial for comprehending the contents of this thesis.

Epidemiology of head and neck cancer

HNC is a rare type of cancer with around 3000 diagnoses per year in the Netherlands[1]. It constitutes a diverse group of cancers affecting the oral cavity, pharynx, larynx, paranasal sinuses, nasal cavity, salivary glands and the unknown primary tumor. The epidemiology of head and neck tumors is intricate and influenced by various factors, including geographical location, lifestyle choices, and exposure to risk factors. The most common risk factors associated with HNC include tobacco use, alcohol consumption, human papillomavirus (HPV) infection, and Epstein-Barr virus (EBV) infection.

Men are diagnosed at a significantly higher rate than women, with ratios typically falling between 2:1 and 4:1[2]. HNC is more common in older individuals, with a mean age of 62 years. However, due the rising incidence of HPV-associated oropharyngeal tumors, the number of younger individuals is also rising[3].

In the Netherlands, more than 1000 patients decease each year due to HNC[4]. Survival is related to tumor stage, where the lower the stage at diagnosis, the higher the survival rates are. The TNM staging system, ranging from I to IV, plays a pivotal role in assessing the extent of disease and guiding treatment decisions in HNC[5]. For most

head and neck tumors, the 5-year relative survival rate has been increasing over the years, although survival remains low for hypopharyngeal cancer. The survival rate for laryngeal cancer remains approximately constant over time[6]. We will delve into two specific HNC types that we studied in this thesis.

Oropharyngeal carcinoma

The oropharyngeal carcinoma is a relatively rare form of cancer that originates in the mucous membrane of the middle throat cavity. The oropharynx is a critical anatomical area within the throat, encompassing structures such as the base of the tongue, the soft palate, the tonsillar regions, and the pharyngeal walls. Given the complexity of this anatomical area, treatment approaches must be precise and conservative to preserve critical functions such as speech and swallowing while minimizing morbidity. Maintaining the patient's quality of life is paramount, underscoring the importance of tailored treatment strategies that address both the cancer and its potential impact on essential physiological processes[7–9].

Symptoms of oropharyngeal carcinoma can vary but often include persistent sore throat, difficulty swallowing (dysphagia), ear pain, a lump in the neck (due to enlarged lymph nodes), and changes in voice or hoarseness. Diagnosis typically involves a comprehensive assessment, including physical examination, imaging studies such as CT scans or MRIs, and biopsy for pathological analysis.

Risk factors for oropharyngeal cancer include smoking, alcohol consumption, and HPV infection. There are notable differences between HPV-positive and HPV-negative tumors. HPV-positive tumors, often found in younger individuals, has a relatively favorable prognosis compared to HPV-negative tumors, which are more commonly associated with traditional risk factors such as tobacco and alcohol use[10]. In the Netherlands, as elsewhere, the epidemiology oropharyngeal cancer has evolved, notably influenced by human papillomavirus (HPV) prevalence[11], making HPV+ tumors more common. This shift has implications for treatment decisions and outcomes.

Treatment for oropharyngeal tumors varies according to the stage of the cancer. For advanced stages (Stage III and IV), where the tumor has spread to nearby lymph nodes or tissues, treatment typically involves a combination of surgery, radiation, and chemotherapy. Chemoradiation is often the primary approach for locally advanced tumors to shrink the tumor and target any spread cancer cells. Surgery may still be considered in certain cases, either before or after chemoradiation, to address remaining tumor or affected lymph nodes[12]. For recurrent or metastatic disease, treatment options may include surgery, radiation therapy, chemotherapy, targeted therapy, or immunotherapy, with a focus on palliative care to alleviate symptoms and improve quality of life[13].

In early-stage tumors (Stage I and II), localized and small tumors may be treated with either surgery or radiation therapy. Surgical options like transoral robotic surgery (TORS) or transoral laser microsurgery (TLM) aim to remove the tumor while preserving healthy surrounding tissue[14]. Alternatively, radiation therapy alone or combined with chemotherapy (chemoradiation) may be used, especially if surgery is not feasible or preferred by the patient. Surgery and radiation have shown to give similar outcomes, but different side-effects[15].

Early stage oropharyngeal carcinoma

Early-stage oropharyngeal cancer, identified at stages I or II, signifies that the cancer is localized within the oropharynx without extensive spread to surrounding tissues or distant sites.

Transoral minimally invasive surgery, may include different surgical techniques, most commonly transoral robotic surgery (TORS) or transoral laser surgery (TOLS). It presents a treatment option for early-stage oropharyngeal cancer that can precisely target and remove the tumor while minimizing damage to surrounding healthy tissues. This approach is particularly suited for patients whose tumors are located in areas accessible through the mouth, allowing for direct visualization and resection of the cancer[16]. Transoral surgery's benefits include a potential reduction in the need for more invasive procedures, a lower risk of disfigurement, and, importantly, the preservation of organ function[17,18]. In the Netherlands it is most often used to avoid radiation if possible. However, when surgery results in too close or positive margins, or when more than very limited neck disease is present, adjuvant radiation therapy or even chemoradiation is necessary to eliminate any residual cancer cells and reduce recurrence risk.

Radiation therapy remains a cornerstone in the management of early-stage oropharyngeal cancer, either as a primary treatment modality or adjuvant following surgery to address microscopic disease. Radiation therapy aims to eradicate cancer cells while preserving as much normal tissue as possible. However, it's associated with toxicities such as dry mouth, dysphagia, and potential long-term changes in salivary function, underscoring the importance of careful treatment planning avoiding large fields and sparing critical structures[19,20].

Because of the side effects of radiotherapy and chemoradiation, de-intensification strategies for eligible patients are being studied widely[21,22]. Controversies persist in determining the optimal treatment approach, yet most researchers concur on one point: if a single modality proves effective, it should be favored over multimodality

treatment. In the case of early stage oropharyngeal tumors, this means that in case of a small, well accessible primary without or with minimal neck disease, surgery is a very good alternative for radiotherapy without risking the long term toxicity of radiotherapy[23].

The choice between radiation and surgery—or the combination thereof—is influenced by several factors, including tumor size, location, neck disease, HPV status, and patient preference. The impact of these treatments on patients varies. TORS, while less invasive than traditional surgery, may still lead to post-operative pain, temporary changes in swallowing, or speech difficulties, though these are generally less severe and resolve more quickly than with open surgical approaches[15]. Radiation therapy, while non-invasive, can cause acute side effects like mucositis, which typically resolve after treatment completion, but it may also lead to long-term changes in saliva production and taste sensation, swallowing problems and long tern fibrosis and atherosclerosis[15].

Choosing the appropriate treatment for early-stage oropharyngeal cancer involves careful consideration of the tumor's size, location, N stage and the HPV status, as well as the patient's overall health and personal preferences. Both TORS and radiation therapy offer the potential for cure with a focus on organ preservation and functional outcomes. Decisions regarding the optimal approach should be made in collaboration with a multidisciplinary team of specialists, ensuring that treatment plans are tailored to achieve the best possible balance between effective cancer control and preservation of quality of life.

Laryngeal cancer

Laryngeal cancer develops in the tissues of the larynx, which is commonly referred to as the voice box. The larynx plays a crucial role in breathing, swallowing, and speaking. Laryngeal cancer can manifest in various parts of the organ, including the vocal cords, supraglottis, glottis and subglottis.

Risk factors for laryngeal cancer include tobacco use, particularly smoking, and excessive alcohol consumption. Chronic exposure to irritants such as industrial chemicals and asbestos, as well as gastroesophageal reflux disease (GERD), may also increase the risk of developing laryngeal cancer.

Symptoms of laryngeal cancer can vary depending on the location and extent of the tumor but often include persistent hoarseness or changes in voice quality, difficulty swallowing (dysphagia), throat pain, ear pain, a lump or mass in the neck, and persistent coughing or coughing up blood[24].

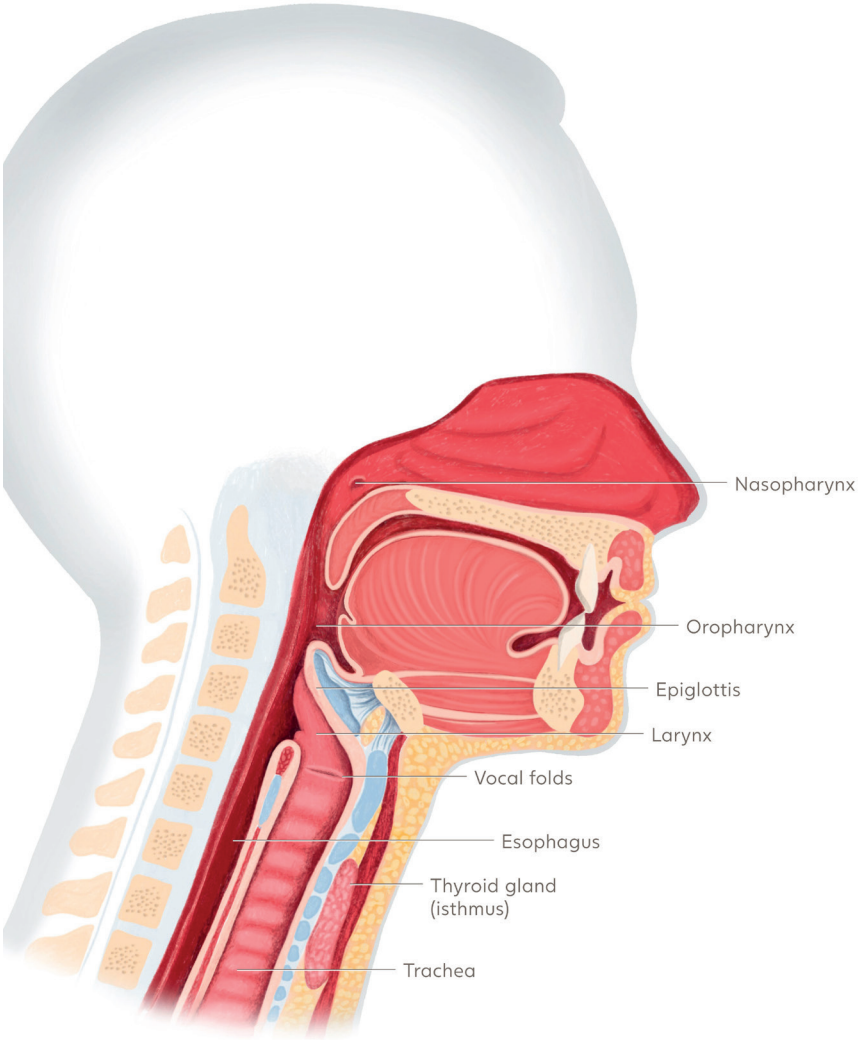

Figure 1. Overview of anatomy of the Head and Neck Region. This image has been used with permission from Atos Medical AB

Treatment options for laryngeal cancer depend on factors such as the stage and location of the tumor, as well as the overall health and preferences of the patient. Treatment for early-stage laryngeal cancer typically involves a combination of surgical and nonsurgical interventions. Surgical options like transoral laser microsurgery (TLM) or partial laryngectomy are commonly employed to remove localized tumors while preserving laryngeal function[25]. Additionally, radiation therapy may be utilized either as a primary treatment modality or in combination with surgery to effectively target cancer cells.

However, in cases of advanced-stage laryngeal cancer, more aggressive approaches such as total laryngectomy or chemoradiation therapy may be necessary to achieve optimal outcomes[26,27]. Treatment decisions should be tailored to each patient's specific circumstances, and require collaboration among a multidisciplinary team of specialists.

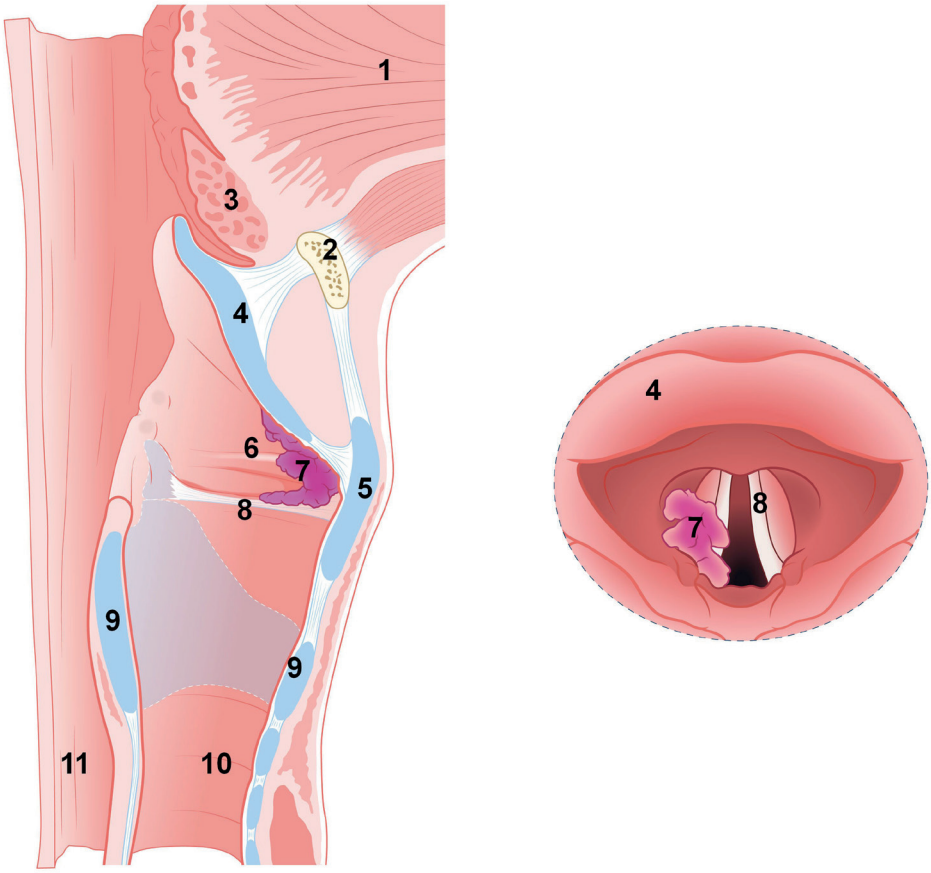

Figure 2. Sagittal overview of the pharynx with a laryngeal tumor

1. tongue, 2. hyoid bone, 3. lingual tonsil, 4. epiglottis, 5. thyroid cartilage, 6. false vocal cord, 7. tumor, 8. true vocal cord, 9. cricoid cartilage, 10. trachea, 11. Esophagus

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Advanced laryngeal cancer

Advanced laryngeal carcinoma represents a severe stage of cancer affecting the larynx, categorized as stage III or IV[28]. Symptoms vary depending on the tumor's location but can include persistent hoarseness, difficulty swallowing, unexplained weight loss, and

in more severe cases, breathing difficulties. The supraglottic area tend to show fewer early symptoms, leading to a higher likelihood of diagnosis at an advanced stage and is particularly prone to lymphatic spread due to the rich lymphatic network, contrasting with glottic cancers, which are often discovered earlier due to voice changes. Subglottic tumor are quite seldom and often precipitates symptoms of dyspnea and coughing, particularly in cases where the tumor attains considerable size, thereby impeding airflow within the respiratory tract.

Treatment options are diverse, with larynx preserving strategies on the one hand, and total laryngectomy (TL) on the other hand. TL, the surgical removal of the entire larynx, is often recommended for extensive tumors, especially T4 or with impaired function at diagnosis or as salvage when other treatments have failed[29,30]. This procedure can effectively control the cancer but results in the loss of natural voice and necessitates a permanent stoma for breathing[31–33]. Respiration is then carried out through a tracheal stoma, created by bringing the trachea to the skin in the lower, front part of the neck. This procedure effectively separates the upper portion of the airway from the lower, leading to permanent loss of voice and smell.

Organ-preserving strategies like chemoradiation (CRT, a combination of cisplatin based chemotherapy and radiation therapy) and radiation therapy alone are preferred when feasible, as they aim to maintain laryngeal function[34]. CRT is particularly used for tumors that are locally or regionally advanced, offering a potential for cure while preserving the larynx[35].

The impact of treatments on patients with advanced laryngeal carcinoma varies significantly. TL, while potentially curative, profoundly affects speech, swallowing, and breathing, necessitating significant lifestyle adjustments and rehabilitation[31]. In most cases, postoperative radiotherapy is still needed. In the Netherlands almost all patient receive a voice prosthesis (VP) during surgery, also called a primary puncture[36]. After rehabilitation most patients are able to use the VP and speak.

Conversely, organ-preserving approaches may lessen these functional impacts but come with their own set of challenges, including acute side effects like mucositis, dysphagia, and altered taste, as well as long-term risks such as radiation-induced fibrosis, swallowing issues and poor laryngeal functioning as well as potentially decreased efficacy in controlling the cancer compared to surgical options[26,37,38]. So, how do you make the right treatment decision?

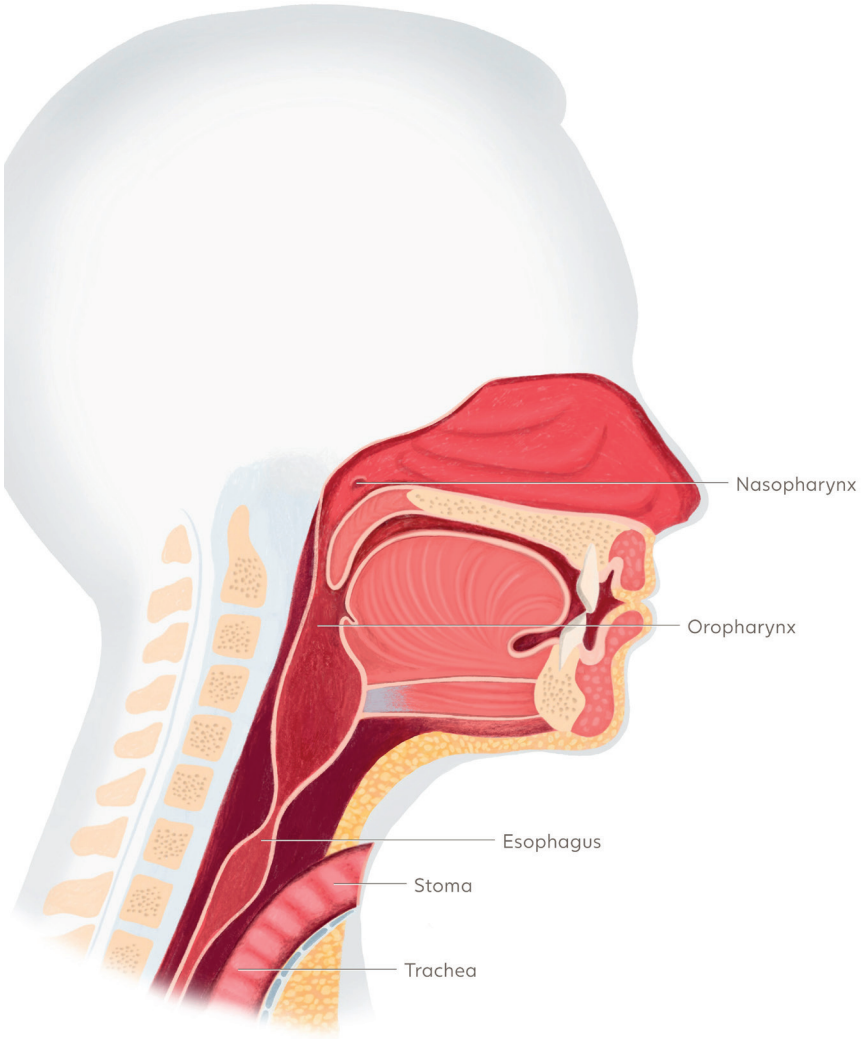

Figure 3. Overview of anatomy after a total laryngectomy. This image has been used with permission from Atos Medical AB

Shared Decision Making

Shared Decision Making (SDM) has evolved from a novel concept to a core component of patient-centered care, emphasizing the partnership between patients and healthcare providers in making health decisions. Initially emerging in the late 20th century in response to a growing recognition of patient autonomy and the ethical imperative for informed consent, SDM has grown in importance as healthcare has become more complex, with an increased focus on patient rights and the recognition that patients'

values and preferences should play a central role in healthcare decisions[39–41]. The benefits of SDM include enhanced patient satisfaction, improved treatment adherence, and a more personalized healthcare experience, particularly in conditions where multiple treatment options exist. However, challenges include time constraints in busy clinical settings, the need for healthcare providers to be skilled in communication and negotiation, and potential increased anxiety in some patients[42,43].

SDM in the medical field is most appropriately applied when patients are faced with decisions involving complex treatment options, multiple possible outcomes, and uncertainty regarding the best course of action. This approach empowers patients to actively participate in their healthcare by collaborating with healthcare professionals to weigh the risks and benefits of different options, leading to decisions that align with their individual circumstances and preferences. It is especially valuable in chronic conditions, end-of-life care, and situations where there are trade-offs between treatment benefits and potential harms. The success of SDM in improving patient outcomes underscores the importance of further research and implementation support[41,44–47]. An established model of SDM consists of three essential components: "team talk," emphasizing support for patients when introducing options and eliciting their goals; "option talk," involving the comparison of alternatives using risk communication principles; and "decision talk," focusing on reaching decisions that reflect informed patient preferences, guided by healthcare professionals' experience and expertise. This model provides a structured framework for collaboration and deliberation in the decision-making process[48].

Decisional conflict arises when individuals face uncertainty and struggle to make choices among various options, particularly when they feel uninformed or uncertain about which option aligns best with their values and preferences. This internal struggle can lead to stress, anxiety, and indecision, hindering the decision-making process and potentially resulting in suboptimal choices[49,50]. Decision regret, on the other hand, occurs when individuals experience negative emotions or dissatisfaction with a decision they have made, often in hindsight. This regret may stem from a perception that an alternative option would have yielded a better outcome or that the chosen course of action did not align with their expectations or values[51,52]. Both decisional conflict and decision regret underscore the importance of effective decision-making processes that prioritize informed choice, active participation, and consideration of individual values and preferences. Shared Decision Making (SDM) aims to address these challenges by fostering collaboration between patients and healthcare providers, providing patients with the information and support they need to make decisions that are aligned with their goals and values, thereby reducing decisional conflict and minimizing the likelihood of decision regret[53].

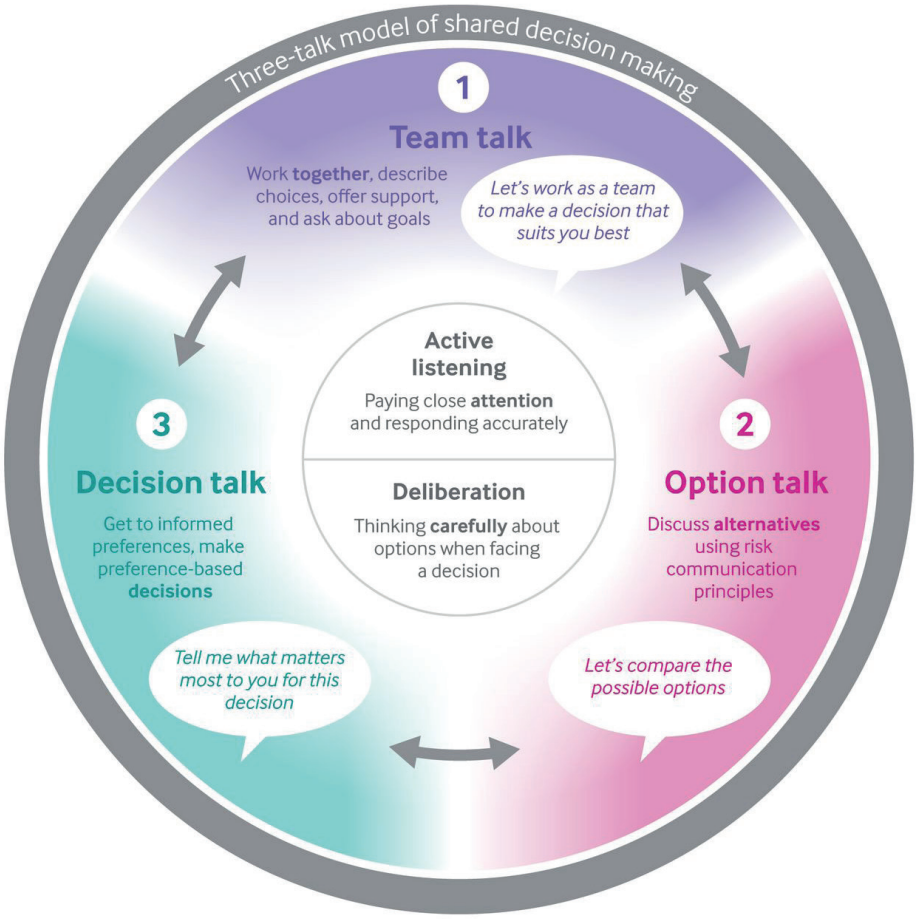

Figure 4. Shared decision making model as developed by Elwyn et al. (2017)[48]

Patients facing HNC treatments should therefore make preference-sensitive decisions, where the trade-offs between treatment efficacy, side effects, and impacts on quality of life are complex and deeply personal. Despite the recognized value of SDM in these cases, research on its application in head and neck oncology is scarce, highlighting a gap in understanding how best to support these patients in their treatment decisions[54].

As mentioned earlier, early-stage oropharyngeal cancer poses preference-sensitive choices between radiation and transoral surgery, while advanced laryngeal cancer presents treatment options with notable side effects and survival trade-offs. We therefore have chosen to investigate these conditions in the context of Patient Decision Aids (PDAs). While our research has primarily focused on the development of a PDA for early-stage oropharyngeal cancer, we have also tested the impact of an earlier developed PDA for advanced laryngeal cancer[55].

Patient decision aids

Patient Decision Aids (PDAs) are instrumental in facilitating Shared Decision Making (SDM), offering a structured approach for patients and healthcare providers to engage in informed discussions about treatment options. PDAs are designed to present evidence-based information about the risks, benefits, and alternatives of treatments, helping patients to make decisions that align with their personal values and preferences[56]. The use of PDAs has been associated with improved knowledge, reduced decisional conflict, and greater satisfaction with the decision-making process. Moreover, PDAs support the implementation of clinical practice guidelines by ensuring that patient choices are informed by the best available evidence[57,58].

Despite benefits, challenges like time constraints and health literacy hinder widespread adoption. Discrepancies exist between positive outcomes and real-world implementation, highlighting a gap between evidence and practice[59]. Additionally, PDAs' availability and efficacy vary, necessitating adherence to International Patient Decision Aid Standards (IPDAS) for evidence-based, patient-centered development[60]. Challenges include managing costs, achieving stakeholder consensus, involving a multidisciplinary team, clinical implementation, and keeping PDAs updated[58,61]. Addressing these demands careful planning, collaboration, and continuous evaluation.

There's a noted discrepancy between the positive outcomes associated with PDA use and the actual implementation of these tools in everyday clinical settings, underscoring a gap between evidence and practice[58,61].

The development of Patient Decision Aids (PDAs) adheres to the International Patient Decision Aid Standards (IPDAS) criteria[60], ensuring evidence-based content, clarity, and patient-centeredness. However, challenges arise, including managing costs effectively, achieving consensus among stakeholders, involving a multidisciplinary team, implementing the PDA into clinical practice seamlessly, and keeping it up to date with evolving evidence and patient preferences. Overcoming these hurdles requires careful planning, collaboration, and continuous evaluation processes.

In head and neck oncology, the lack of PDAs underscores a pressing necessity for tailored tools that address the distinctive decision-making challenges faced by patients. Bridging this gap is imperative for propelling patient-centered care forward in oncology, enabling patients to be fully informed and empowered in their treatment decisions.

Once a treatment plan, such as a total laryngectomy for advanced laryngeal cancer, has been chosen, patients will enter a rehabilitation phase. The following section of this introduction will explore particular aspects of rehabilitation tailored to laryngectomized patients.

Rehabilitation after Total Laryngectomy

Rehabilitation after TL presents a profound challenge for patients, affecting their ability to speak, breathe, and swallow. This multifaceted rehabilitation process aims to address these challenges, focusing on restoring respiratory function, facilitating communication, and ensuring nutritional support. In addition, physical rehabilitation is also an important aspect to take into account. Essential components of the first challenges involves the use of voice prostheses (VP) and Heat and Moisture Exchangers (HMEs)[62]

Voice prosthesis

Vocal rehabilitation after TL is a crucial component of post-surgical care, aimed at restoring the patient's ability to communicate verbally. In the Western world, tracheoesophageal puncture (TEP) with voice prosthesis (VP) insertion has emerged as the gold standard for voice restoration following TL. This method significantly surpasses other techniques in providing patients with more intelligible speech and better voice quality[63]. Indwelling voice prostheses, including the Provox, Fahl and Blom-Singer models, are the most common types used, categorized into regular VPs for standard cases and problem-solving VPs for those with specific issues such as short device lifetimes or periprosthetic leakage[36,64].

The device lifetime of VPs varies, typically ranging from 2 to 6 months, depending on several factors such as the type of VP, patient's ability to maintain the device, biological factors like biofilm formation on the prosthesis as well as reimbursement and other barriers for the patient. The primary reason for VP replacement is transprosthetic leakage, occurring in 55% to 80% of cases, followed by periprosthetic leakage affecting 5% to 30% of patients[64]. These frequent replacements can significantly impact a patient's quality of life, leading to feelings of insecurity and unplanned hospital visits[65,66].

Despite the challenges associated with VPs, the use of tracheoesophageal voice prosthesis remains a highly effective method for vocal rehabilitation post-TL. Research and development continue to aim for VPs with longer lifetimes and fewer complications, improving patient satisfaction and quality of life. The ongoing innovation in this field underscores the importance of tailored approaches to vocal rehabilitation, ensuring that each patient receives the most suitable device based on their individual needs and circumstances[67].

Heat and Moisture Exchangers

Respiratory rehabilitation after TL is essential due to the separation of the upper and lower respiratory tracts, fundamentally altering the airway dynamics. After the surgery, the natural functions of the upper airway—warming, humidifying, and filtering the inhaled air—are bypassed as breathing is redirected through a stoma directly into the lower airways. This loss leads to increased pulmonary symptoms such as involuntary coughing, mucus retention, and forced expectoration. Furthermore, patients are at a higher risk of airway infections and inflammations, affecting not only their physical health but also their sleep, social interactions, and overall quality of life[68–72].

To mitigate these challenges, two primary devices have been developed: stoma cloth covers (bib) and Heat and Moisture Exchangers (HMEs). While bibs are a cost-effective solution offering potentially good air conditioning, they pose challenges in stoma occlusion for speech and are generally less favored by patients[73]. Consequently, HMEs have become the preferred choice in many developed countries due to their efficiency in retaining heat and moisture from exhaled air and transferring it to the inhaled air, significantly improving the tracheal climate, reducing coughing and sputum production, and enhancing patients' quality of life[68,74–76].These devices, attached via an adhesive baseplate or cannula over the stoma, have shown efficacy in long-term use by preventing the deterioration of tracheal cells and even restoring them.

Despite the benefits, the performance of HMEs is balanced against their resistance, which can vary based on the device's size and internal specifications. Higher resistance HMEs, while more effective in air conditioning, may cause discomfort during physical activities, potentially discouraging physical exercise and impacting overall health and quality of life negatively[77].

The choice of HME, therefore, should consider individual patient needs, lifestyle, and the specific level of activity to ensure optimal compliance and enhance the quality of life. With a range of HMEs available, tailored to offer varying levels of resistance and humidification, it's crucial for patients to find a balance that supports their respiratory health without compromising their activity levels and overall well-being[78].

Cardiopulmonary exercise testing

Maximal Cardiopulmonary Exercise Testing (CPET) is a valuable tool in rehabilitation, offering insights into patients' cardiovascular and pulmonary health, as well as overall physical fitness. It is typically conducted in a controlled clinical setting under the supervision of healthcare professionals. During the test, patients are instructed to perform incremental exercise on a stationary cycle or treadmill. The intensity of exercise gradually increases in predetermined stages or through continuous ramp protocols[79].

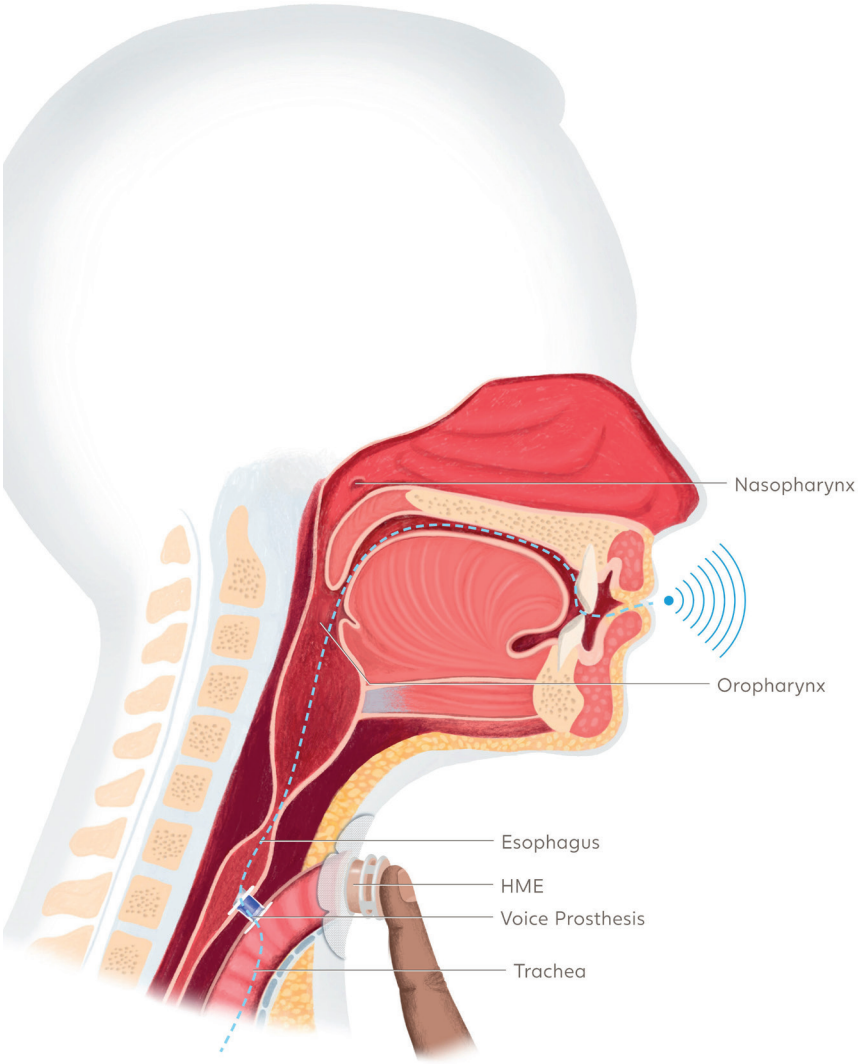

Figure 5. Overview of a laryngectomized patient with a voiceprosthesis and HME. This image has been used with permission from Atos Medical AB.

Throughout the test, various physiological parameters are continuously monitored. These include heart rate, oxygen consumption (VO2), carbon dioxide production (VCO2), minute ventilation (VE), respiratory exchange ratio (RER) and electrocardiography (ECG). A key aspect of maximal CPET is the utilization of a face mask or mouthpiece connected to a metabolic cart, which allows for the collection of expired gases. This equipment enables the accurate measurement of respiratory parameters, providing insights into the efficiency of gas exchange during exercise[80].

Despite its proven benefits, maximal CPET has not found widespread use in laryngectomy rehabilitation. This may be attributed to the intensive focus on other aspects of rehabilitation, such as vocal rehabilitation, which often take precedence due to their immediate impact on quality of life. However, with advancements in medical care, laryngectomy patients are now surviving longer, leading to an increased need for comprehensive rehabilitation strategies. Incorporating maximal CPET into laryngectomy rehabilitation could provide crucial information about patients' aerobic capacity and exercise tolerance, aiding in the optimization of their overall functional capacity and quality of life.

Nevertheless, integrating this presents unique challenges. One significant obstacle is the use of a face mask during the test, which is essential for accurate measurement of respiratory parameters but is not useful for laryngectomy patients since their airway ends in their neck after surgery. This difficulty in using traditional CPET equipment highlights the need for innovative approaches and adaptations to make maximal CPET accessible and beneficial for laryngectomy patients. Overcoming these challenges could unlock the potential of maximal CPET as a valuable tool in optimizing the rehabilitation outcomes and long-term well-being of laryngectomy patients.

Overview and aims of this thesis

This thesis is divided into two parts, each dedicated to distinct yet interconnected aspects of head-and-neck cancer (HNC) care. The first part focuses on shared decision-making dynamics, specifically examining advanced laryngeal cancer and operable oropharyngeal carcinoma. It aims to provide insights into the prevalence of decisional conflict and decision regret among head-and-neck oncology patients, exploring whether enhanced counseling can reduce these issues while also augmenting knowledge. Additionally, this part investigates the development and impact of patient decision aids (PDAs) in facilitating informed decision-making processes. The second part centers on rehabilitation strategies tailored to patients undergoing Total Laryngectomy (TL). The aim of this part is to contribute to the advancement of knowledge regarding rehabilitation techniques and assistive devices, with the ultimate goal of improving outcomes for TL patients.

Part 1: Shared Decision Making in Head and Neck Oncology

Chapter 2 presents a systematic review and meta-analysis, delving into the current literature on the prevalence of decisional conflict and decision regret among individuals diagnosed with head-and-neck cancer. Through an exhaustive examination of existing research, we aimed to provide a comprehensive understanding of the challenges faced by patients in making treatment decisions. In **Chapter 3**, we shifted our focus inward

to explore the level of observed and perceived shared decision-making among head-and-neck surgeons, patients, and their relatives within our own institute. By assessing the dynamics of decision-making processes in a localized setting, we aimed to gain insights into potential areas for improvement and optimization of patient care. Moving forward to **Chapter 4**, our attention turned specifically to patients with advanced laryngeal carcinoma who are confronted with curative treatment options. This investigation is a component of a larger multicenter study aimed at evaluating the impact of a patient decision aid tailored to this particular patient cohort. By examining the level of decisional conflict experienced by these individuals, we sought to ascertain the efficacy of interventions designed to support informed decision-making. **Chapter 5** of this thesis investigated the impact of a Patient Decision Aid (PDA) for individuals facing advanced laryngeal cancer. We assessed how this tool influences treatment knowledge, decisional conflict and perceived shared decision-making. Finally, **Chapter 6** details our efforts in the development of a PDA tailored specifically for individuals diagnosed with operable oropharyngeal carcinoma. By customizing decision support tools to address the unique needs and preferences of this patient population, we aimed to empower patients to actively participate in the decision-making process regarding their treatment options.

Part 2: Rehabilitation after Total Laryngectomy

Voice prostheses are crucial for laryngectomized patients, but they come with a limited device lifetime. In **Chapter 7**, we thoroughly explored the feasibility of prophylactic replacement strategies to address this challenge. **Chapter 8** examined a newly developed voice prosthesis, meant to overcome biofilm destruction of the valve, focusing on its acceptance and voice quality among laryngectomized patients, providing valuable insights into its efficacy and usability. Moving forward to **Chapter 9**, we delved into the feasibility of Maximal Cardiopulmonary Exercise testing in laryngectomized patients, aiming to understand the physiological responses to exercise within this population. Additionally, we investigated the influence of Heat and Moisture Exchangers (HMEs) on exercise responses, shedding light on potential optimization strategies for respiratory health post-laryngectomy. And even after total laryngectomy, patients can still possess remarkable abilities. In **Chapter 10**, we shared an uplifting anecdote through a letter to the editor, highlighting the inspiring story of a laryngectomized patient who defies expectations by demonstrating an extraordinary ability to sing and play guitar.

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Part 1

Shared Decision Making in Head and Neck Oncology

Chapter 2

Decisional Conflict and Decision Regret in Head and Neck Oncology – A Systematic Review and Meta-Analysis

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Abstract

Importance: Head-and-Neck cancer (HNC) often requires treatment with major impact on quality of life (QoL). Treatment decision-making is often challenging, as it involves balancing survival against the preservation of QoL, and choosing among treatments with comparable outcomes but variation in morbidity and adverse events. Consequently, the potential for decisional conflict (DC) and decision regret (DR) is high.

Objective: This systematic review summarizes the literature on DC and DR in HNC, to give an overview of its prevalence and extent, and to advice on clinical practice and future research.

Data sources: We searched Embase.com, Web of Science, MEDLINE, and PsycINFO up to 24-02-2023, including all years of publication.

Study Selection: Eligible studies addressed DC and/or DR as primary or secondary outcome with any instrument in HNC, except cutaneous tumors. Two mutually blinded researchers conducted screening and inclusion with support of Rayyan software's AI assistant and conducted Risk of Bias (ROB) assessment.

Data Extraction and Synthesis: PRISMA guidelines were followed for data-extraction. RoB were done using CASP (qualitative) and CLARITY (quantitative). Meta-analysis with a random-effects model was considered to obtain pooled prevalence estimates for DC and DR when at least four sufficiently clinically homogeneous studies were available.

Main Outcomes and Measures: Prevalence of DC (qualitative, Decisional Conflict Scale, SURE questionnaire) and DR (qualitative, study-specific questionnaires, Decision Regret Scale, Shame and Stigma Scale).

Results: Twenty-eight studies were included, with sixteen included in meta-analyses for DR prevalence. The pooled prevalence of clinically relevant DR above cut-off score for validated questionnaires (eleven studies, n=2053) was 71% (95% CI 58% – 82%, I^2 = 94%), while for study-specific questionnaires (fives studies, n=674) it was 11% (95% CI 5% – 22%, I^2 =92%). This suggests study-specific questionnaires underestimate DR. Only four studies investigated DC, showing a prevalence of 22.6-47.5% above cut-off values. Derived overarching themes found in qualitative studies were "preparation", "SDM roles", "information", "time pressure", "stress of diagnosis" and "consequences".

Conclusions and Relevance: Although limited data on DC and DR are available, the studies performed indicate that DC and DR are highly prevalent issues in HNC. This underscores the rationale to improve counseling and shared decision-making for this patient population.

Introduction

Head-and-neck cancer (HNC) often requires complex treatment. The head-and-neck area houses numerous vital anatomical structures responsible for essential functions like speaking, breathing, eating, and swallowing. During HNC treatment, these structures may be damaged, leading to functional impairments. In addition, HNC treatment can lead to disfigurement. These side-effects lead to a deterioration of Quality of Life (QoL)[1].

HNC is often curable when treated in an early stage, whereas advanced stages of disease have a higher mortality rate and also significantly higher morbidity[2,3]. HNC is a rare and aggressive disease in which numerous difficult decisions must be made based on relatively limited information and time[4]. Also, there is a trade-off between survival and QoL[5].

When making a treatment choice, patients can experience decisional conflict (DC). DC is a state of uncertainty that arises when a person faces a challenging decision with competing options, and feels unsure about which choice to make[6,7]. DC has many negative consequences, such as delay in decision-making, making treatment choices that are not in line with patients' preferences, and decisional regret[11,12].

Decisional regret (DR) is a negative feeling associated with grief, disappointment, or distress following a decision regarding healthcare. DR is a complex construct that is associated with multiple variables such as socio-demographics, disease, side-effects, chosen treatment, but primarily with DC and received information[13–15]. DR may have serious consequences such as decline in QoL, incomplete recovery from treatment, and depression[13,16]. Given the complex nature of the decisions to be made in HNC, and the many risk factors predisposing for DC and DR that are often present in this patient population, such as lower health literacy, frailty, and psychosocial problems[17,18], DC is looming and the potential for developing DR is high.

This systematic review aims to provide an overview of the current literature on DC and DR in HNC patients, and to obtain reliable estimates of prevalence and degree. Such insights are important for guiding advice on clinical practice and future research.

Methods

Study design

This is a systematic review about DC and DR in HNC patients, reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines[19]. The review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) database prior to starting the search (CRD42021267872).

Literature search process

A sensitive literature search was developed with support of a medical librarian and adapted for the following databases: MEDLINE (Ovid), Embase, PsycINFO (Ovid), and Web of Science.

The search strategy, with a final search on 24 February 2023, included terms relating to HNC and DC and/or DR and consisted of both database-specific thesaurus terms (where applicable) and terms to search in the title, abstract and keywords. The simplified structure of the search was: (head and neck cancer) AND (decisional conflict OR decisional regret). See appendix A for full details of the search strategy. No restrictions on language or publication period were applied. References of the included articles were checked to identify any potentially relevant missed publications.

Inclusion criteria

Eligible studies were quantitative, qualitative, or mixed-methods studies addressing DC and/or DR in patients with HNC of any stage and receiving any treatment. DC and DR could be primary or secondary outcomes and be measured with any instrument, including study-specific questionnaires. Studies with subjects < 18 years old, conference abstracts, and studies on cutaneous carcinomas were excluded.

Selection process

After deduplication, all identified records were uploaded into Rayyan software[20]. Because of the high yield of our search, we used Rayyan's Artificial Intelligence (AI) to support screening[21]. The Rayyan AI algorithm calculates the likelihood of eligibility for records, based on a first set of manual inclusions (training data). Potential eligibility of new records is represented on a 0-5 stars scale, with 5 stars indicating the highest likelihood for eligibility.

To avoid missing any relevant record, we manually screened 50% of all records, focusing on keywords 'regret,' 'conflict,' or 'shared-decision making' in title or abstract, before letting Rayyan rate the remaining records. Next, we manually screened 2000 records in descending rating order, after which ratings were recalculated for the remainder. Of those, we manually screened all 2.5 star records, and a random sample of 10% of the lower-rated records.

All records were screened by two mutually blinded researchers (AH and DJ or CA). Included articles were labeled by topic (DR or DC), study design and tumor location. Discrepancies were solved by consensus.

Data extraction

Data extraction included author, year of publication, study type, study population, tumor location(s), tumor stage, treatment modalities, methods of measurement for DR and DC, and all reported data regarding DR and DC. Since studies used different scales and measures for point estimates and dispersion (due to different underlying distributions), which would prohibit useful meta-analysis, we used a dichotomous outcome (present yes/no) for the meta-analyses. Where needed, authors were contacted for data regarding the prevalence of DC and/or DR in their sample.

Quality and Risk of Bias Appraisal

All appraisals were done by two mutually blinded researchers (AH and DJ or CA) and were discussed until consensus. For quantitative research designs, we used the CLARITY checklist for assessing Risk of Bias (RoB) in Cross-Sectional Surveys[23]. This 5-item tool addresses population, response rate, missing data, clinical sensibility, reliability, and validity of the survey instrument. We rated the RoB for the reliability and validity items as low if a study used a scale that had been (previously) validated.

The CASP Qualitative Studies Checklist was used for qualitative studies[24]. This 10-item checklist consists of three sections pertaining to the validity, results, and the extent to which the results are valuable for the context in which the study is used.

Data synthesis and statistical analysis

Data from qualitative studies was analyzed through inductive content analysis[25]. Themes as reported were extracted and coded by AH. In a group meeting (AH, CA, DJ), similar but differently worded themes were combined under a single term. Overlap between themes were examined, and themes describing different, but related concepts were merged into a higher-order overarching theme. Finally, we examined overall saturation of the data.

When at least four sufficiently homogeneous quantitative studies were available, we calculated pooled prevalence estimates for DC and DR, using the GLMM model because of high variance in events and sample sizes[26]. Since considerable heterogeneity was expected, considering different tumor locations and treatments, as well as differences between countries and hospitals, we adopted a random-effects model. The between-study component of variance τ^2 was estimated by use of the DerSimonian–Laird method. Subgroup analyses were performed on type of used instrument. All analysis were done in R (version 4.2.2) and Rstudio, using packages 'meta'[27] and 'metafor'[28].

Results

Study selection

The search yielded 27.258 records. Following deduplication, 16.009 unique articles remained. Of the manually screened first 50% of records, 178 publications were retained for full-text screening. Rayyan ratings for the remaining records (n=7180) ranged from 4.5 stars (n=1), 3.5 stars (n=66) to 2.5 stars and lower (n= 7113). After screening the 2000 highest ranked records, the 4.5-stars and thirteen of the 3.5-stars records were retained for full-text screening. After score recalculation, the 660 records with a 2.5 star rating were screened, and none included. After a second recalculation, the remaining 4520 articles received ≤ 1.5 stars. Of these, 500 random records (>10%) were screened, without any inclusions, after which the remaining records were discarded.

Thus, 192 studies were retained for full-text review, of which 164 were subsequently excluded, mostly because of ineligible outcomes (n=105), leaving a total of 28 included studies for data extraction. See figure 1.

Description of included studies

Of the 28 included studies, five had a qualitative design (DC=3, DR=1, DC and DR=1) and 23 were quantitative (DC=3, DR=19, DC and DR=1). Publication dates ranged from 1980 to 2022, and twelve studies were < 5 years old.

Two quantitative studies reported on the same study using different but overlapping subsamples (Windon et al[29,30]); only the data from the larger study was used for meta-analysis[29].

For ten quantitative studies, we contacted the authors for additional data regarding the prevalence of DR. For two, the raw data were no longer available (Gill et al.[31], Shuman et al.[32]). One study by Shaverdian et al.[33] considered DR of a de-escalation treatment instead of regular treatment, and we excluded this study from the meta-analysis on grounds of clinical heterogeneity. Hence, meta-analyses were performed on sixteen articles, using three different instruments (Appendix B): study-specific questionnaires, the Shame and Stigma Scale (SSS) and the Decision Regret Scale (DRS).

Qualitative studies (N=5)

Risk of Bias

Three of the five qualitative studies had a low RoB[30,34,35]. All had clear aims and a thorough method. One article[36] did not comment on the relation between researcher and study participants. Another article[37] did not have dedicated results and discussion sections and was therefore rated as high RoB (Table 1).

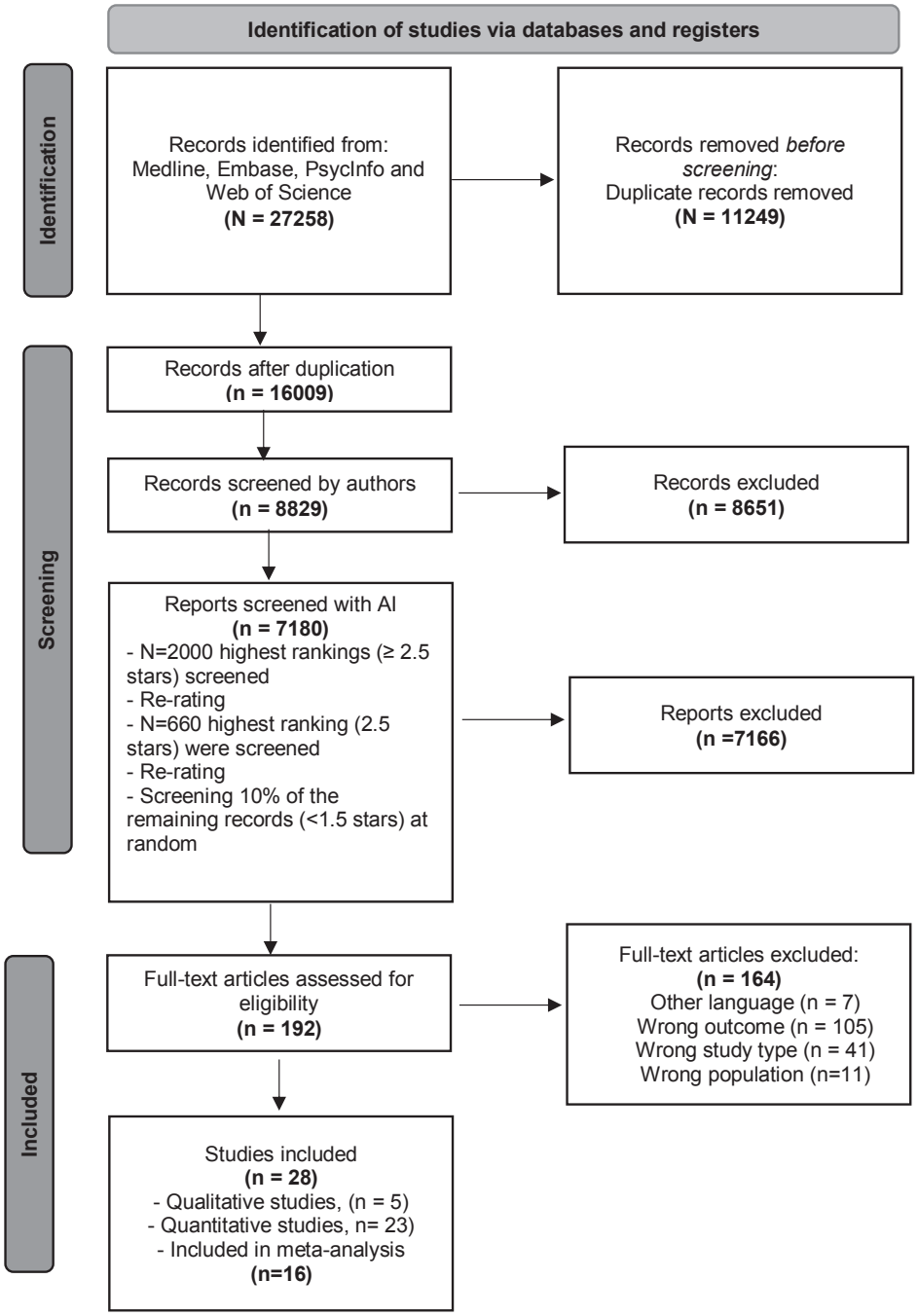


Figure 1. Prisma flow diagram

Data synthesis

For all five articles, DC and DR were secondary outcomes, and without evidence for data saturation. The participants in the four qualitative studies investigating DC mentioned that time pressure, emotions, receiving too much and too complicated information, and a lack of practical information, caused DC[30,35–37]. Derived overarching themes relating to DC were "preparation", "SDM roles", "information", "time pressure", and "stress of diagnosis".

Derived themes relating to DR were "consequences", which included altered appearance, depression and functional consequences, and "ambivalence". See table 2 for all results.

Quantitative studies (N=23)

Risk of Bias

All 23 studies had representative populations (table 1). Seventeen studies had a low RoB. Most uncertainties were due to inadequate reporting on missing data and response rates. Overall, studies using study-specific questionnaires had a higher RoB compared to studies using validated questionnaires. Studies published prior to 2010[38–41] were less consequent in reporting information necessary for assessing RoB.

Decisional Conflict

Of the four included studies[32,42–44], three used the Decisional Conflict Scale (DCS)[11]. One study only included laryngeal carcinomas and found a mean DCS score of 25.6 (range 0-78)[32]. The authors had no access to the raw data to obtain prevalence. The two other studies included multiple HNC sites and found DC prevalence of 33.3% and 47.5%, respectively[42,43]. The fourth study used the SURE-questionnaire[45] and found that 22.6% of patients reported DC[44]. We refrained from meta-analysis since there were only four studies, using two types of instruments (Table 3, Appendix B).

Decisional Regret

Three different instruments were used in the twenty studies assessing DR (see Appendix B and Table 3): study specific questionnaires (n=5[38–41,46]), the Shame and Stigma Scale (SSS) (n=4[47–50]), and the Decision Regret Scale (DRS) (n=11[29–33,51–56]).

Study specific questionnaires

All five papers that used a study specific questionnaire reported prevalence as primary outcome. Four were relatively old studies (1987-2009)[38–41], one was from 2022[46], and samples ranged from 76-273 participants. One of these studies investigated DR after surgical treatment for laryngeal cancer[39], and one after commando operation[46]. The other three papers reported on a mix of HNC sites and treatments, but all in an advanced tumor stage[38,40,41]. Overall, the prevalence of DR ranged from 5.1% to 35.5%.

Shame and Stigma Scale (SSS)

Three out of four studies using the SSS included a mix of tumors and stages[47–49], one only included nasopharyngeal tumors[50]. The study populations varied from 42-219 participants. All authors provided additional data, with prevalence of DR ranging from 72.1% to 85.8%.

Decision Regret Scale (DRS)

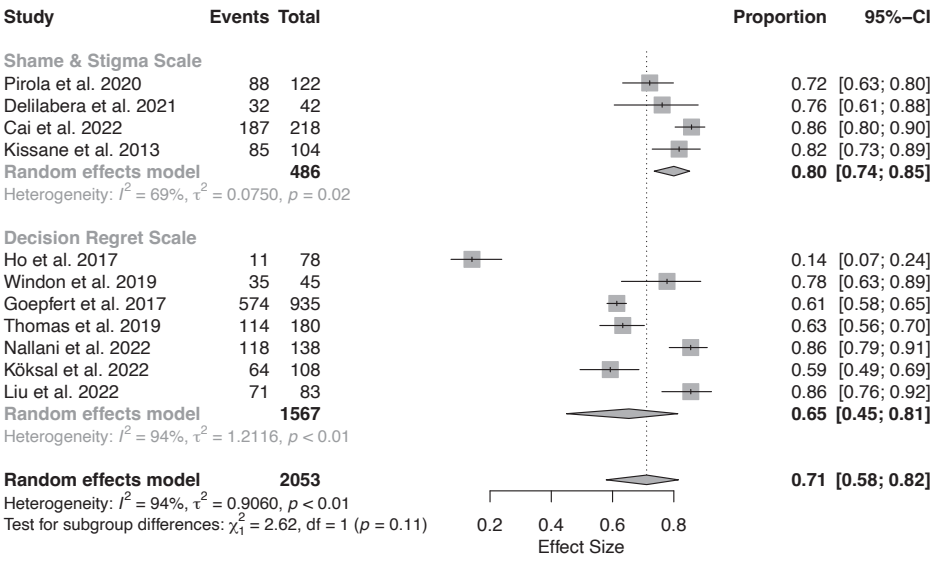
The studies using the DRS (n=11) were published between 2010 and 2022[29–33,51–56]. Most studies included all tumor stages, and a mix of treatments. Four studies used prevalence to report DR[33,51–53], of which one studied the level of DR after choosing de-escalation treatment instead of regular treatment and found that nobody experienced regret[33]. Upon our request, five[30,52,54–56] of the eight[30–33,52,54–56] authors approached provided additional data for calculating prevalence estimates. With exclusion of the de-escalation treatment study[33], the prevalence of DR varied from 14.2% to 85.5% (median 61.4%). The lowest prevalence was reported in a study investigating DR in patients that had received radiation for nasopharyngeal tumors[52].

Meta-analysis of the prevalence of Decisional Regret

Data of sixteen studies were included in the meta-analyses, with in total 2727 participants of whom 1452 had DR. We performed separate meta-analyses for the data of study-specific questionnaires (n=5) and data of validated questionnaires (N=11), the latter including a subgroup analysis for the SSS and DRS results.

The meta-analysis of validated questionnaires showed significant high heterogeneity (I^2 = 94%) between studies (see figure 2A). The overall pooled DR prevalence was 71% (95% CI 58% – 82%). One outlier (Ho et al.[52]), concerned DR in nasopharyngeal carcinoma patients receiving radiation therapy and reported a markedly lower prevalence (14%). Sensitivity analysis excluding this study reduced DRS-subgroup heterogeneity by only 5% (to 89%) and did not have a meaningful impact on the overall results.

Meta-analysis of the study specific questionnaire group (N=5) showed a significant and high heterogeneity (I^2 = 92%, see figure 2B), with pooled DR prevalence of 11% (95% CI 5% – 22%).



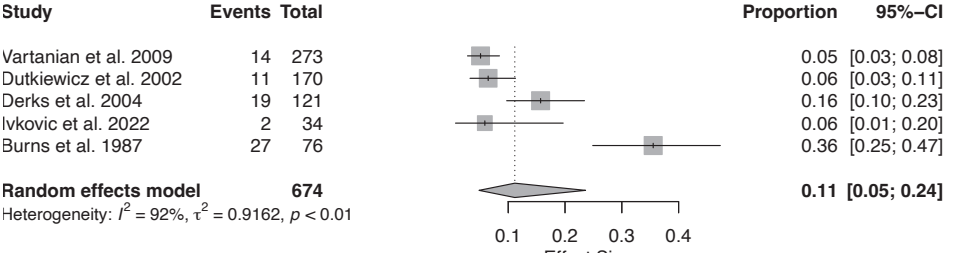


Figure 2. Forest plot of pooled prevalence of Decisional Regret

2A. Forest plot of validated questionnaires: SSS and DRS.

2B. Forest plot of study-specific questionnaires

Table 1. Risk of Bias: Qualitative (CASP) and Quantitative (CLARITY)

Qualitative studies	**CASP question**				
Author (year)	**1. Clear aim of research?**	**2. Appropriate methodology?**	**3. Appropriate design?**	**4. Appropriate recruitment strategy?**	**5. Appropriate data collection?**
Noonan et al[34]. (2010)	Yes	Yes	Yes	Yes	Yes
Gibson et al[36]. (2021)	Yes	Yes	Yes	Yes	Yes
Edwards et al[37]. (1998)	Yes	Yes	Yes	Yes	Yes
Bisschop et al[35]. (2017)	Yes	Yes	Yes	Yes	Yes
Windon et al[30]. (2021)	Yes	Yes	Yes	Yes	Yes

Quantitative studies	**CLARITY question**	
Author (year)	**1. Is the source population representative of the population of interest?**	**2. Is the response rate adequate?**
Panda et al[42]. (2020)	Probably yes	Definitely yes
Hoesseini et al[43]. (2022)	Probably yes	Definitely yes
Wamkpha et al[44]. (2021)	Probably yes	Definitely no
Shuman et al[32]. (2017)	Probably yes	Definitely yes
Burns et al[38]. (1987)	Probably yes	Probably no
Dutkiewicz et al[39]. (2002)	Probably yes	Probably no
Derks et al[40]. (2004)	Probably yes	Definitely yes
Vartanian et al[41]. (2009)	Probably yes	Probably no
Ivkovic et al.[46] (2022)	Probably yes	Probably no
Kissane et al[47]. (2013)	Probably yes	Definitely yes
Pirola et al[48]. (2020)	Probably yes	Definitely yes
Delilabera et al[49]. (2021)	Probably yes	Probably yes
Cai et al[50]. (2022)	Probably yes	Probably no
Gill et al[31]. (2010)	Probably yes	Definitely yes
Goepfert et al[51]. (2017)	Probably yes	Probably no
Ho et al[52]. (2017)	Probably yes	Definitely yes
Thomas et al[53]. (2019)	Probably yes	Definitely yes
Shaverdian et al[33]. (2019)	Probably yes	Definitely yes

CASP question					
6. Researcher-participant relationship described?	**7. Considered ethical issues?**	**8. Rigorous data analysis?**	**9. Clear statement of findings?**	**10. Is the research valuable?**	**Overall RoB assessment**
Yes	Yes	Yes	Yes	Yes	Low
No	Yes	Yes	Yes	Yes	Medium
Yes	Yes	Yes	No	No	High
Yes	Yes	Yes	Yes	Yes	Low
Yes	Yes	Yes	Yes	Yes	Low

CLARITY question			
3. Is there little missing data?	**4. Is the survey clinically sensible?**	**5. Is there evidence for the reliability and validity of the instrument?**	**Overall RoB assessment**
Definitely yes	Definitely yes	Definitely yes	Low
Definitely yes	Definitely yes	Definitely yes	Low
Definitely yes	Definitely yes	Definitely yes	Low/medium
Definitely yes	Definitely yes	Definitely yes	Low
Probably no	Probably no	Definitely no	High
Probably yes	Probably no	Definitely no	Medium/high
Probably no	Probably no	Definitely no	Medium/high
Probably yes	Probably no	Definitely no	Medium/high
Probably yes	Definitely no	Definitely no	High
Probably no	Definitely yes	Definitely yes	Low
Definitely yes	Definitely yes	Definitely yes	Low
Probably no	Definitely yes	Definitely yes	Low
Definitely yes	Probably yes	Definitely yes	Low
Definitely yes	Probably yes	Probably yes	Low
Definitely yes	Definitely yes	Definitely yes	Low
Unanswerable*	Definitely yes	Definitely yes	Low
Probably yes	Definitely yes	Definitely yes	Low
Probably yes	Definitely yes	Definitely yes	Low

Table 1. Continued

Quantitative studies	CLARITY question	
Author (year)	**1. Is the source population representative of the population of interest?**	**2. Is the response rate adequate?**
Windon et al[30]. (2019)	Probably yes	Probably no
Windon et al[29]. (2019)	Probably yes	Probably yes
Nallani et al[54]. (2022)	Probably yes	Definitely yes
Köksal et al[56]. (2022)	Probably yes	Definitely yes
Liu et al[55]. (2022)	Probably yes	Definitely yes

*This is a 'letter to the editor', all questions were answered except nr. 3.

Table 2. Results qualitative studies

Article	Study aim	Tumor location	Tumor stage	Treatment
Noonan et al[34]. 2010	To describe the experience of total laryngectomy from patients' perspectives.	Larynx	-	Laryngectomy
Gibson et al[36]. 2021	To explore the experience of survivors of head and neck cancer, with a focus on the psychosocial impact of altered appearance.	Head and Neck*	-	Surgery, radiation, chemotherapy
Edwards et al[37]. 1998	To find out wat patients, their families and professionals thought of head and neck cancer services.	Head and Neck *	-	-

	CLARITY question			
	3. Is there little missing data?	**4. Is the survey clinically sensible?**	**5. Is there evidence for the reliability and validity of the instrument?**	**Overall RoB assessment**
	Probably yes	Definitely yes	Definitely yes	Low
	Probably no	Definitely yes	Definitely yes	Low
	Probably yes	Definitely yes	Definitely yes	Low
	Definitely yes	Definitely yes	Definitely yes	Low
	Probably no	Definitely yes	Definitely yes	Low

	Participants	**Reported themes**	**Construct**	**Deduced themes**
	10	1. Psychological concerns: Depression; Regrets; Personal resolve 2. Functional difficulties: Physical; Speech	DR	- Consequences - Ambivalence
	21	1. Preparation: decision-making; preparation for altered appearance 2. Consequences: reactions from others; adapting to altered appearance 3. Altered Appearance: weight loss; face, skin and hair changes; reconstructive surgery	DR DC	- Consequences - Preparation - Information - SDM roles - Ambivalence
	22 patients, 11 relatives	1. Choice: treatment; involvement 2. Information (understanding) 3. Psychological Support 4. Hospital accommodation 5. Co-ordination and administrative difficulties 6. Teamwork	DC	- SDM roles - Information - Stress of diagnosis - Time pressure

Table 2. Results qualitative studies

Article	Study aim	Tumor location	Tumor stage	Treatment
Bisschop et al[35]. 2017	To investigate the experiences and preferences within a group of Head-and-Neck Oncology patients, to fill the gap in existing knowledge	Oral cavity, oropharynx, larynx	I-IV	-
Windon et al[30]. 2021	To describe the experiences and needs of patients making decisions regarding primary treatment for their oropharyngeal cancer.	Oropharynx	I-IV	CRT, Surgery, Surgery + RT, Surgery + CRT

DR = Decision Regret, DC = Decisional Conflict, CRT = chemoradiotherapy, RT = radiation therapy, SDM = Shared Decision Making

*Not otherwise specified

Participants	Reported themes	Construct	Deduced themes
19	1. Information, communication and education 2. Respect for patients' values, preferences and expressed needs 3. Involvement of family and friends 4. Emotional support and alleviation of fear and anxiety 5. Coordination and integration of care 6. Physical comfort	DC	- Preparation - Information - SDM roles
11 pre-treatment patients, 15 post-treatment patients	1. Emotional response: alarm at cancer diagnosis; decisional conflict 2. Roles in decision-making: trust in treatment team; shared decision with doctor, team; shared decision with spouse; ultimately decisional autonomy 3. Other factors influencing treatment decision-making: desire for physical tumor removal; fear of adverse effects of treatment; possible need for adjuvant therapy obviated advantage of surgery; patient-specific values 4. Informational needs: felt generally well-informed; patient-centered information would be helpful; internet is a poor resource for information-gathering; advantage of hearing from post-treatment survivors	DC	- Stress of diagnosis - Preparation - Information - Time pressure - SDM roles

Table 3. Quantitative results

Decisional Conflict			
Author (year)	**Tumor location**	**Stage**	**Treatment**
Shuman et al[32]. (2017)	Larynx	I-IV	Surgery, radiation, chemotherapy
Panda et al[42]. (2020)	Head and Neck*	-	Surgery, radiation, chemotherapy
Hoesseini et al[43]. (2023)	Larynx, oropharynx, oral cavity, hypopharynx, nasopharynx, parotid gland	I-IV	Surgery, radiation, chemotherapy
Wamkpha et al[44]. (2021)	Head and Neck*	-	Surgery
Decision Regret			
Author (year)	**Tumor location**	**Stage**	**Treatment**
Burns et al[38]. (1987)	Larynx, oral cavity, pharynx, paranasal sinuses	IV	Surgery, radiation, chemotherapy, adjuvant (C)RT
Dutkiewicz et al[39]. (2002)	Larynx	-	Surgery: partial and total laryngectomy
Derks et al[40]. (2004)	Larynx, oral cavity, pharynx	II-IV	Surgery, radiation, chemotherapy, adjuvant (C)RT
Vartanian et al[41]. (2009)	Larynx, oral cavity, oropharynx, hypopharynx	T3, T4	Surgery, adjuvant RT
Ivkovic et al.[46] (2022)	Oral cavity	III-IV	Commando procedure
Kissane et al[47]. (2013)	Oral cavity, pharynx, larynx	I-IV	Surgery
Pirola et al[48]. (2020)	Oral cavity, pharynx, larynx, nasal cavity, thyroid	-	-
Delilabera et al[49]. (2021)	Oral cavity, pharynx, larynx, unknown primary	I-IV	Surgery, radiation, chemotherapy, adjuvant (C)RT

N	Questionnaire	Results
57	DCS	Mean 25.6, range 0-78, SD 20.1
27	DCS	DCS < 25 n=18 (66.7%) DCS ≥ 25 n=9 (33.3%)
263	DCS	DCS < 25 n=138 (52.5%) DCS ≥ 25 n=125 (47.5%) DCS ≥ 25-37.5 n=87 (33.1%) DCS ≥ 37.5 n=38 (14.4%)
53	SURE	DC absent n= 41 (77.4%) DC present n= 12 (22.6%)

N	Questionnaire	Results	Levels of regret, N (%)	Regret no/yes, N (%)
76	Study specific	27/76 (35.5%) patients experienced DR		No 49 (64.5%) Yes 27 (35.5%)
170	Study specific	11/170 (6.4%) patients experienced DR		No 159 (93.6%) Yes 11 (6.4%)
121	Study specific	19/121 (15.7%) patients experienced DR	No 102 (84.3%) Mild 5 (4.1%) Moderate-strong 14 (11.6%)	No 102 (84.3%) Yes 19 (15.7%)
273	Study specific	14/273 (5.1%) patients experienced DR		No 259 (94.9%) Yes 14 (5.1%)
34	Study specific	2/34 (5.9%) patients experienced DR		No 32 (94.1%) Yes 2 (5.9%)
104	SSS	Mean 29.45, SD 23.94 Median 25, IQR 8.3-41.7	No 19 (18.3%) Mild 37 (35.6%) Moderate-strong 48 (46.1%)	No 19 (18.3%) Yes 85 (81.7%)
122	SSS	Mean 32.04, SD 28.7 Median 25, IQR 0-58.3	No 34 (27.9%) Mild 29 (23.8%) Moderate-strong 59 (48.3%)	No 34 (27.9%) Yes 88 (72.1%)
42	SSS	Mean 39.3, SD 33.1	No 10 (23.8%) Mild 7 (16.7%) Moderate-strong 25 (59.5%)	No 10 (23.8%) Yes 32 (76.2%)

Table 3. Quantitative results

Decision Regret Author (year)	Tumor location	Stage	Treatment
Cai et al.[50] (2022)	Nasopharynx	I-IV	-
Gill et al[31]. (2010)	Head and Neck*	-	Radiation
Shuman et al[32]. (2017)	Larynx	I-IV	Surgery, radiation, chemotherapy
Goepfert et al[51]. (2017)	Oropharynx	I-IV	Surgery, radiation, chemotherapy, adjuvant (C)RT
Ho et al[52]. (2017)	Nasopharynx	-	Radiation
Thomas et al[53]. (2019)	Head and Neck*	-	-
Shaverdian et al.(2019)	Head and Neck cancer not otherwise specified	-	De-escalation chemoradiation
Windon et al[29]. (2019)	Oropharynx, oral cavity, larynx	0-IV	Surgery, radiation, chemotherapy, adjuvant (C)RT
Windon et al[30]. (2019) Ψ	Oropharynx	I-IV	Surgery, radiation, chemotherapy, adjuvant (C)RT
Nallani et al[54]. (2022)	Oral cavity, oropharynx, hypopharynx, larynx	O-IV	Surgery, radiation, chemotherapy, adjuvant (C)RT
Liu et al[55]. (2022)	-	-	Head and neck reconstruction with fibular or scapular free flaps

N	Questionnaire	Results	Levels of regret, N (%)	Regret no/yes, N (%)
218	SSS	Mean 32.8, SD 24.8, Median 31.3, IQR 12.5-50	No 31 (14.2%) Mild 74 (33.9%) Moderate-strong 113 (51.9%)	No 31 (14.2%) Yes 187 (85.8%)
30	DRS	Mean 12.33, SD 14.37, range 0-50		
57	DRS	Mean 16.2, SD 17.3, range 0-60		
935	DRS	Mean 12.7, SD 16.3	No 361 (38.6%) Mild 428 (45.8%) Moderate-strong 146 (15.6%)	No 361 (38.6%) Yes 574 (61.4%)
78	DRS		No 66 (85.8%) Mild 7 (9.0%) Moderate-strong 4 (5.2%)	No 67 (85.8%) Yes 11 (14.2%)
180/274	DRS	Mean 18.2, range 0-09	No 66 (36.7%) Mild 66 (36.7%) Moderate-strong 48 (26.7%)	No 66 (36.7%) Yes 114 (63.3%)
27	DRS			No 27 (100%) Yes 0 (0%)
45/150	DRS	Median 5; IQR 0-25	No 20 (44.5%) Mild 15 (33.3%) Moderate-strong 10 (22.2%)	No 20 (44.5%) Yes 35 (55.5%)
37	DRS	Median 5; IQR 0-20		
138/140	DRS	Three months post-treatment (n=138): Median 20, IQR 10-30	No 20 (15.7%) Mild 76 (54.3%) Moderate-strong 42 (30.0%)	No 20 (15.7%) Yes 118 (84.3%)
83	DRS	FFF: Mean 22.7; SD 20.6 SCF: Mean 19.2; SD 20.1	No 12 (14.5%) Mild 42 (50.6%) Moderate-strong 29 (34.9%)	No 12 (14.5%) Yes 71 (85.5%)

Table 3. Quantitative results

Decision Regret Author (year)	Tumor location	Stage	Treatment
Köksal et al[56]. (2022)	Nasopharynx, oropharynx, hypopharynx, larynx, oral cavity, sinuses, salivary glands		Surgery, radiation, chemotherapy, adjuvant (C)RT

CRT = chemoradiotherapy, RT = radiation therapy, FFF = Fibula Free Flaps, SCF = Scapula Free Flaps, DCS = Decisional Conflict Scale, SURE: Sure of myself; Understand information; Risk-benefit ratio; Encouragement, DR = Decision Regret, SSS = Shame and Stigma Scale, DRS = Decision Regret Scale

N	Questionnaire	Results	Levels of regret, N (%)	Regret no/yes, N (%)
108	DRS	Mean 23.94; SD 32.36	No 44 (40.5%) Mild 33 (30.1%) Moderate-strong 31 (29.4%)	No 44 (40.5%) Yes 64 (59.5%)

*Not otherwise specified Ψ The second paper of Windon et al.[30] used a subgroup of oropharyngeal cancer patients from the earlier published article[29]. Thus, the second article was not included in the meta-analysis.

Discussion

With this systematic review, we aimed to provide a comprehensive overview of the quantitative and qualitative research on decisional conflict (DC) and decisional regret (DR) in Head-and-Neck cancer (HNC) patients. Overall, the results suggest that DC and DR are common in HNC patients and that the impact of DC and DR on these patients is substantial.

Quality and completeness of the evidence

A limited number of studies have been conducted over the years (1987-2022), with more studies in later years. However, research regarding this topic in HNC lags compared to more prevalent cancers.

Overall, the available studies are of good methodological quality, with the most pertinent risk of bias resulting from low response rates and the use of non-validated questionnaires. Notably, the validated questionnaires used in the included studies have also not been evaluated specifically for use in a HNC population. Detailed reporting on the timing of the measurement of DC and DR was lacking. The inclusion criteria and measurement instruments differ across studies and results are heterogeneous. Risks of bias may, in part, result from DC and DR being secondary outcomes in many of the included studies.

Main Results

Decisional Conflict

Between 1 in 4 and 1 in 2 HNC patients reported DC. Although patients with HNC generally have poorer prognosis, more psychosocial problems, and lower health literacy, these figures are comparable, or slightly lower, to the prevalence of DC in prostate cancer patients (23% to 61%[15,57–61]) and breast cancer patients (33-67%[62–66]), which have been studied more intensively. Further research is needed to obtain more reliable estimates of DC prevalence in HNC patients.

Qualitative studies indicated that the stress of the diagnosis and lack of clear information regarding disease, treatments, and their impact, led to a high level of DC in most patients. Experienced lack of SDM made patients feel objectified. However, when patients did experience SDM, it was not always clear to them what their role was, which then led to additional uncertainty. Although we cannot know what level of SDM was applied, the results suggest a need for better implementation of SDM.

Increased attention to SDM has led to the development of patient decision aids. Such aids might overcome most of the issues leading to DC as mentioned by participants in the qualitative studies. Evidence suggests that patient decision aids can lead to a clinically meaningful reduction of DC[57,58,67,68]. To date, only a few decision aids have been developed for patients with HNC, and impact evaluations of these tools are not yet available[69,70].

Decision Regret

Compared to DC, DR has been studied more extensively. The prevalence of DR in the available studies differs vastly, ranging from 0%-86%. The type of measurement instrument clearly influences observed prevalence: study-specific questionnaires all showed a low prevalence (5-36%) whereas the validated questionnaires show evidently higher prevalence (SSS 72-86% and DRS 14-86%), suggesting underestimation of DR when using unvalidated questionnaires.

DRS results were highly heterogeneous. Removing the outlier[52] on nasopharyngeal cancer did not improve heterogeneity and had limited impact on results. The six other studies using the DRS consisted of a variety of HN tumors, stages, and treatments. Although we hypothesize that tumor location, stage, received treatments, timing of measurement, and the occurrence of complications or poor outcomes influence the level of DR, the available studies prohibit comparisons of clinical subgroups due to the inclusion of mixed populations and limited reporting on these variables. Therefore, we were unable to explain the observed heterogeneity, and the pooled estimate of DR prevalence should be interpreted with caution. A recent systematic review investigating the extent and risk factors of DR after a variety of healthcare decisions showed that DR prevalence is higher in more complex or life-threatening diseases[16]. The authors reported that risk factors related to the decision-making process (e.g., DC, satisfaction with information provided, role in decision-making) were most important, followed by treatment related factors (e.g., complications, adverse outcomes) and rarely sociodemographic characteristics (e.g., age, education). However, the review did not include studies on HNC and future research is needed to identify risk factors for DR in the HNC population.

Limitations of the review process

We used a highly sensitive search to identify all possible studies. To manage the vast number of records retrieved, we used an AI-supported inclusion process. As a result, we did not manually screen all identified records. However, we used a very conservative approach, using a much higher than minimally recommended number of manual inclusion decisions[22], and screening a substantial amount of records with a 2.0 star rating or less. At a 2.5 star rating as threshold for exclusion, sensitivity of Rayyan's AI method is reported to be 100%. We therefore believe it is unlikely that we have missed relevant publications.

Conclusion

This systematic review of decisional conflict (DC) and decision regret (DR) in head-and-neck cancer (HNC) patients highlights the limited and heterogeneous nature of research in this area, but also indicates that DC and DR are highly prevalent and have a substantial impact on patients' life. More research is needed to investigate risk factors for DC and DR in HNC patients, and to enhance counseling strategies and SDM tools, aiming at reducing DC and DR.

Appendix B: Additional information on the measurement instruments

Decisional Conflict Scale (DCS)[11]

This scale consists of 16 statements with 5 response categories (strongly agree to strongly disagree). Although there is no official cut-off point, the most commonly used cut-off considered to indicate DC is a score greater than or equal to 25 points[71].

SURE questionnaire[45]

This questionnaire contains four items that can be scored with yes (1 point) or no (0 points). Scores below 4 points are considered to indicate clinically significant decisional conflict[72].

Shame and Stigma Scale (SSS) [47,73]

The SSS was developed to measure the impact of treatment for head-and-neck cancer on the Quality of Life of patients through four specific domains: shame with appearance (8 items), sense of stigma (6 items), regrets (3 items) and social concerns (3 items). The total and subscales scores are calculated by summing the responses to the relevant items and then multiplying the sum by a scaling constant [100 / (4 * number of items on scale). Scores range from 0 (not at all) to 100 (a lot). All domains can be used separately, so we used the scores of the regret domain as score for decision regret.

Decision Regret Scale (DRS)[74]

The DRS was developed in 1996 and has been validated for multiple fields and widely used for many years. The DRS consists of five statements with five answer options ranging from strongly agree to strongly disagree. Scores are converted to a 0-100 scale, where a score of 0 means no regret; a score of 100 means high regret[75].

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Chapter 3

Exploring the State of Shared Decision-Making in Head and Neck Oncology: Assessing Treatment Communication

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Minor revisions: Patient Education and Counseling

Abstract

Objective. To explore the state of shared decision-making (SDM) in head and neck (HN) oncology by investigating the extent to which SDM is currently employed by HN surgeons and how the perceived levels of SDM relate to the observed levels of SDM. Additionally, surgeon and patient perspectives on patient involvement in SDM and potential associations with observed levels of SDM were explored.

Methods. Perceived level of SDM and patient involvement were measured by SDM-Q-9/ SDM-Q-Doc resp. Control Preference Scale. Observed SDM was measured by analyzing audiotaped consultations (N=42) using the OPTION^{mcc+}. Univariate linear analyses were conducted to identify possible associations with surgeon-observed SDM.

Results. Median perceived SDM scores of surgeons (74.4%) and patients (71.1%) were relatively high, whereas observed median OPTION-scores were moderate (surgeons 48%, patients 42%, caregivers 24%). Consultation time and patient OPTION-score were positively associated with surgeon OPTION-score.

Conclusion. Surgeons and patients overestimate the extent of SDM compared to the observed reality. Patients' goals, values and preferences need to be addressed more during consultations.

Practice Implications. The findings can be used to raise awareness of SDM among surgeons to improve their skills. Routine training in medical education can benefit from effective integration of SDM principles during consultations.

Keywords: Shared decision-making; Head and Neck Oncology; Patient involvement; Participation; Patient-provider communication; OPTION^{mcc}; Treatment decision-making; Preferences; Care goals, Values

Introduction

The dynamic, collaborative process of shared decision-making (SDM) allows patients, and when present, informal caregivers (hereafter: caregivers), to be involved during consultations[1-4]. Particularly important in applying SDM is the prioritization of the patient's needs, values, goals of care, and preferences. When it comes to health- or treatment-related decisions, SDM has demonstrated several benefits, such as reducing the likelihood of decisional regret, higher patient satisfaction, lower healthcare costs, and ultimately potentially higher quality of life (QoL)[5-10]. Because of SDM, patients are generally better informed about benefits and risks, enabling healthcare providers and patients to choose treatment options that best suit patient needs[1-4].

In recent years, there has been a significant drive towards SDM in oncology healthcare. Patients are increasingly being viewed as partners, rather than passive recipients of treatment[11]. However, the implementation of SDM often proves to be challenging due to several factors, such as consultation time[12], uncertainty or lack of consensus regarding the preferred treatment choice, or healthcare providers' limited communication skills[13]. In addition, patients' preferences for involvement in the decision-making process may differ significantly from the healthcare provider's view of these preferences. Previous research has shown that patients' preferences and perceptions of their involvement in decision-making vary[14]. Some patients prefer active involvement, while others opt for a more passive role[14, 15]. The application of SDM should acknowledge these potential differences by requiring healthcare providers to step in as mediators in order to collaboratively make treatment decisions[16]. Nevertheless, healthcare providers often find it difficult to involve patients in decision-making[17, 18]. Meanwhile, patients and their caregivers may encounter barriers that hinder their participation in the decision-making process, including limited knowledge as well as underestimating their own expertise relative to that of healthcare providers[19, 20]. Patients' belief in the "doctor knows best" concept might pose significant hurdles in making collaborative treatment decisions. Consequently, weighing the potential benefits of treatment against the potential impact on their QoL is often very complex.

Especially in the context of head and neck cancer (HNC), a delicate consideration of the potential advantages and drawbacks of each treatment option remains crucial, as comprehensive aggressive treatments, including surgery, radiation therapy and chemotherapy are frequently required[21]. These treatment modalities can have a major impact on patients' QoL by potentially causing significant functional impairments related to speaking, swallowing, eating, or breathing[22-24]. Moreover, patients may experience pain, fatigue, and emotional distress, which can further affect their overall

well-being[25]. The overarching goal of most treatments is to cure patients from their malignancy, but there is often a delicate balance between extending survival and preserving QoL[23, 26]. Consequently, in these situations, the implementation of SDM is important to value the patients' personal values, goals of care, needs, and preferences.

Despite the fact that SDM is particularly suitable for HNC, its implementation remains insufficiently explored. This represents an essential knowledge gap, as it has been documented that HNC patients experience clinically significant decisional conflict and regret[27-31], despite initially being satisfied with the treatment decision[32]. As such, we need to clarify two issues. First, information is lacking on the extent to which healthcare providers within HNC presently apply SDM. Second, it remains unknown to what extent head and neck (HN) healthcare providers and patients perceive SDM being employed during consultation, and how these observed and perceived levels of SDM relate to each other. Only two prior studies that have assessed SDM implementation have taken into account both the perceived level of SDM of healthcare providers and patients, while also investigating the observed level of SDM[33, 34]. Accordingly, with this study, we aim to explore SDM in HN oncology by (1) investigating the extent to which surgeons employ SDM in daily practice, and (2) by gaining insight into how the perceived level of SDM by surgeons and patients relates to observed SDM. Additionally, we examine patient preferences for SDM and the extent to which surgeons can properly assess them.

Methods

This prospective cross-sectional study was conducted according to the principles of the Declaration of Helsinki at the Department of Head and Neck Oncology and Surgery at a Dutch tertiary hospital [35]. The ethical review committee approved the study (registration number IRBd21-078). The research design, data collection process, and anticipated analyses were preregistered on the Open Science Framework (OSF; https://osf.io/248fu/).

Participants and procedure

We recruited five out of ten experienced HN surgeons based on age and gender to form a representative group within the Head and Neck department. Inclusion criteria were: 1) performing clinical work for more than three days per week; 2) having a permanent position as HN surgeon; and 3) having treatment decision-making consultations with non-cutaneous carcinoma HNC patients. Surgeons involved in the study setup were excluded as potential participants (RD, MvdB). To be eligible for the study, patients had to 1) be diagnosed with a primary non-cutaneous HNC; 2) be eighteen years or older; 3) have sufficient command of the Dutch language, and 4) no cognitive impairments (e.g., Korsakov syndrome). Patients were screened by the multidisciplinary tumor board, and then contacted by one of the researchers (AH or SD) to be informed about the study. Interested patients were seen before consultation for a face-to-face explanation of the study and the opportunity to ask questions, after which they signed informed consent.

Between May 2021 and October 2022, consultations between surgeons, patients, and if present, their caregivers were recorded with a Roland Ediroll R-07[36]. During these consultations, diagnosis and advice for treatment from the multidisciplinary tumor board were discussed. Following up on previous studies[33, 34, 37-41], we aimed to obtain at least five recordings per surgeon.

Measures

Patients' age, gender, and diagnosis were collected from their electronic health record. Other characteristics, such as marital status, living situation, education level, employment status, and presence of an informal caregiver, were obtained after consultation via a study specific questionnaire that included the Dutch version of the SDM-Q-9 for patients and the Control Preference Scale (CPS)[42]. Likewise, after consultation, HN surgeons completed a similar study specific questionnaire, including questions about their work experience in Head and Neck oncology (in years), training in SDM (none, minimal= attended at least one course/training, some= attended > 2 courses/trainings), the SDM-Q-Doc for healthcare providers, and an adjusted CPS to fit surgeons' perspective.

The Dutch versions of the SDM-Q-9 and SDM-Q-Doc (Appendix A) have previously shown to be reliable instruments for investigating how SDM is perceived[43-45]. Both are nine-item, validated questionnaires that measure patients' and surgeons' perceived level of SDM on a six-point Likert scale, ranging from 0 (completely disagree) to 5 (completely agree). Scores can be summed up, averaged, and then rescaled into a percentage range from 0 (no perceived SDM) to 100 (highest level of perceived SDM). In addition, the validated Control Preference Scale (CPS) was used to assess patients' preference for and perceived involvement in the decision-making process. The scale contains five decision-making related statements, with two describing an active role of the patient (patient-led), one a shared role (collaborative), and two a passive role of the patient (physician-led), which we reduced into three categories for analysis[46, 47]. We developed two customized CPS measures alongside Degner's original: one to assess surgeons' perception of patients' preference and another to measure their own preference for patient involvement in decision-making.

For objective assessment of the level of SDM, the validated Observing Patient Involvement (OPTION) scale was used. The original OPTION[5] manual[48], in which only healthcare providers are assessed, was not specific enough as SDM should also allow the patient and their caregivers to actively participate in conversation[49]. For this reason, we used the OPTION^{mcc} manual[50] and adapted it for our study, the OPTION^{mcc+} (Appendix B). Instead of scoring patients and caregivers from 0 (passive participation) to 2 (active participation), they were assessed similarly to the surgeons on a 5-point scale. The seven OPTION items were scored based on the general description in the manual wherein scores for surgeons range from 0 (no effort) to 4 (exemplary effort) and scores for patients and caregivers from 0 (passive participation) to 4 (very active participation). Before actual assessment of the consultations, two raters (SD and RT) performed a calibration session. Each scored ten randomly chosen consultations independently to discuss any discrepancies in OPTION-scores to reach consensus. The OPTION-scores (0-28) of both raters were summed, averaged and then rescaled into a percentage total score between zero and hundred[50]. There are no officially defined cutoff values to interpret the observed level of SDM, but some studies have used three categories[34, 39]: low (0-33.3%), moderate (33.3-66.6%), and high (66.6-100%), which we adopted.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics 27[51], with a significance level set at $p < 0.05$. Only consultations with both surgeon's and patient's questionnaires were included for analysis. Descriptive data were employed in accordance with the normal distribution of the data. Before analysis of the data, the two-way mixed inter-rater reliability, single measurement intra-class correlations coefficients (ICC) with a

consistency agreement and 95% confidence interval (CI) were calculated[52]. Following the OPTION manual, an ICC score of > 0.6 was deemed to be acceptable to continue independent scoring by the two raters[48]. When ICC was ≤ 0.6, calibration between the raters was continued until ICC > 0.6 was achieved.

A Bland-Altman plot was created to examine the consistency between the SDM-Q-9 and SDM-Q-Doc questionnaires, thereby providing insight into potential systematic discrepancies and the extent of the differences in scores. To investigate any potential associations with surgeons' OPTION-scores, univariate linear regression analyses were conducted for the variables: consultation duration, patients' age, education level, tumor location, tumor stage, SDM-Q-9 score, SDM-Q-Doc score, CPS, the presence of a caregiver, and caregivers' OPTION-score. Multivariate linear regression was not performed due to the lack of statistical power.

Results

Five surgeons conducted 42 audiotaped consultations. Six consultations were excluded because questionnaires were not returned, leaving 36 consultations for analysis (Figure 1). The median duration of the consultations was 20 minutes (range 10-43 minutes). Most patients were male (25/36), and the mean age was 67.8 years (SD 2.0). Sixteen patients were diagnosed with an early stage of disease (stage I and II), and the predominant types of carcinoma were oral (10/36) and oropharyngeal (10/36). Most of the HN surgeons were male (4 out of 5), and their working experience ranged from 15 to 40 years. Only one surgeon had followed multiple courses on SDM (the only female) and two others had completed an SDM-related course, whilst the remaining two had no experience or training in SDM. Table 2 presents a full overview of characteristics.

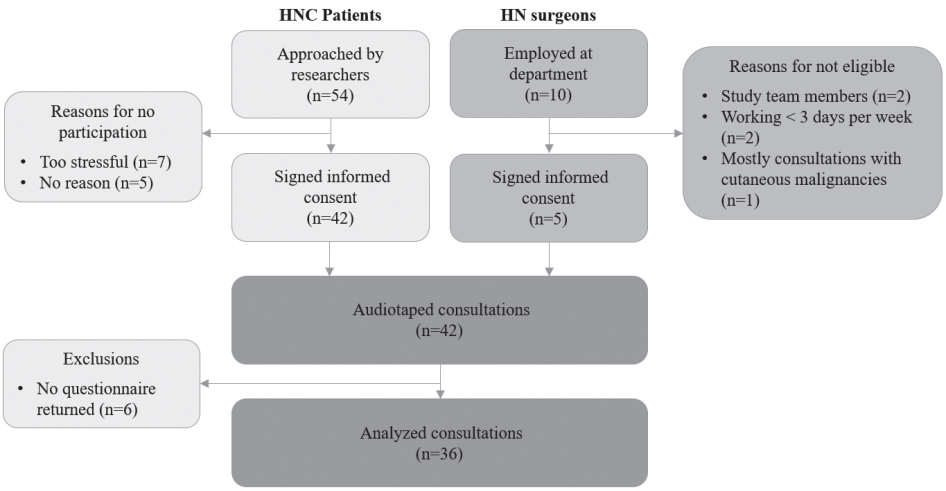


Figure 1. Flowchart of study inclusions

Observed levels of SDM

Inter-rater reliability

Reliability calculations, including the ten calibration consultations, resulted in a good level of agreement with ICCs of 0.767 (surgeons) 0.762 (patients) and 0.809 (caregivers).

OPTION-scores

The median total OPTION-score for all surgeons was 48.0%, and ranged between 9.0 and 95.0 percent. OPTION-scores varied widely between the five surgeons. Three surgeons scored substantially lower for observed SDM level than perceived based on the SDM-Q-Doc and SDM-Q-9 (Appendix C). When looking at the item level (Table 2), surgeons

scored moderate on all items, except for item 4 'option talk' on which they scored high. The median total OPTION-score for patients was 42% (range 0-91%). Patients scored low on item 2 'alternative option talk', and moderate on all other items. The median total OPTION-score for caregivers was 24% (range 0-64), with no median scores above 37.5% on all seven items. Appendices D and E provide a visual representation of the OPTION-scores per individual group and per item.

Table 1. Baseline characteristics of patients and surgeons

Patients	**N=36**
Age in years (mean, SD)	67.8 (2.0)
Gender	
Male	25 (70%)
Female	11 (30%)
Educational level	
Low	15 (42%)
Middle	10 (28%)
High	11 (30%)
Tumor stage	
I	9 (25%)
II	7 (19%)
III	11 (31%)
IV	9 (25%)
Tumor location	
Hypopharynx	2 (6%)
Larynx	4 (11%)
Oral cavity	10 (28%)
Oropharynx	10 (28%)
CUP	3 (8%)
Nasopharynx	2 (6%)
Parotic gland	2 (6%)
Vestibulum nasi*	3 (8%)
Treatment undergone	
Surgery	17 (48%)
(+ PORT)	*4*
Chemo-radiation	7 (19%)
Radiation therapy	9 (25%)
None	3 (8%)

Table 1. Baseline characteristics of patients and surgeons

Patients	**N=36**
Intention chosen treatment	
Curative	33 (92%)
Palliative	3 (8%)
Treatment according to protocol	
Yes	35 (97%)
No	1 (3%)
Reason	Patient's wish
Duration of consultation in minutes (median, range)	20,15 (10,05 – 43,23)
Visiting primary physician	
Yes	9 (25%)
No	27 (75%)
Brought to consultation	
Came alone	7 (19%)
Partner	16 (44%)
Child(ren)	6 (17%)
Friend	2 (6%)
Sibling	1 (3%)
Partner and child(ren)	1 (3%)
Other**	3 (8%)
Head-and-Neck Surgeons	N=5
Age in years (median, range)	54 (39 – 63)
Gender	
Male	4 (80%)
Female	1 (20%)
Work experience in years (median, range)	24 (15 – 40)
Training in SDM	
None	2 (40%)
Minimal	2 (40%)
Some	1 (20%)

Note: *Of which one had a mucosal melanoma; **Others were daughter in law, partner's cousin, child, and sibling; CUP = Carcinoma of an unknown primary tumor; SDM = shared decision-making; PORT = postoperative radiation treatment

Table 2. OPTION-scores per item

Item	Behavior description	Surgeons Median (range)	Patients Median (range)	Relatives Median (range)
1	Goal talk: identify patient values and goals of care	37.5% (0-75.0%)	50.0%, (0-100%)	25.0% (0-75.0%)
2	Alternative option talk: discussion of alternate options	50.0% (0-100%)	25.0% (0-100%)	25.0% (0-75.0%)
3	Team talk: forming a partnership	62.5% (12.5-100%)	50.0% (0-100%)	37.5% (0-75.0%)
4	Option talk: information about options	75.0% (12.5-100%)	50.0% (0-100%)	37.5% (0-75.0%)
5	Decision talk: eliciting patient's preferences	50.0% (0-100%)	50.0% (0-100%)	37.5% (0-87.5.0%)
6	Integrative decision talk: integrating patient's preferences	43.8% (0-100%)	43.8% (0-100%)	25.0% (0-75.0%)
7	Evaluation talk: check satisfaction with choice and SDM process	37.5% (0-100%)	37.5% (0-100%)	25.0% (0-75.0%)

Note: The categories are indicated in colors: low score is white (score between 0% and 33.3%), moderate score is light grey (score between 33.3% and 66.6%), and high score is dark grey (score between 66.6% and 100%).

Perceived levels of SDM

The surgeons gave themselves a median SDM-Q-Doc score of 71.1%, with a wide range (26.7-91%). None of them rated themselves the maximum 100% score (Appendix F). The highest median score was observed for item 9 'agreement' with a score of five points, while items 7 'weighing' and 8 'decision' had the lowest median scores of three points. Similarly, patients had a median SDM-Q-9 score of 74.4% (range 8.9-100%). A quarter of the patients (9/36) rated the consultation with the maximum SDM-Q-9 score (100%). Item 5 'understanding' received the highest median score of five points, while items 6 'preference' and 7 'weighing' scored the lowest with a median of 3.5 points. Appendix G presents the scoring on the SDM-Q-Doc and SDM-Q-9 per item.

When comparing scores for the perceived level of SDM, a Bland-Altman analysis showed that the SDM-Q-9 scores were significantly higher than the SDM-Q-Doc scores, with a small mean difference of 2.5%. However, also several opposing scores were observed. The plot can be found in Appendix H.

Patient involvement in SDM process and surgeon's perspective (CPS)
Based on the CPS scored, most patients (n=17, 47.2%) expressed a preference for a collaborative treatment choice, followed by a physician-controlled choice (n=11, 30.6%). Surgeons also predominantly favored a collaborated choice (n=16, 44.4%), with a patient-controlled choice (n=13, 36.1%) being the next most common option.

In twenty-three cases (63.9%), the surgeon's assumptions aligned with patient preferences for involvement, but in thirteen cases (36.1%), there was a mismatch. Among cases where surgeons assumed a patient-controlled approach (n=13), one patient actually preferred collaboration, while five patients favored a physician-controlled approach. Conversely, in cases where surgeons assumed a collaborative approach (n=15), one patient desired a patient-controlled approach, and two preferred a physician-controlled one. Additionally, when surgeons assumed patients preferred physician-controlled decision-making (n=7), four patients preferred a collaborative decision-making process.

In nine of 42 consultations (21.4%), the way in which the consultation had taken place did not match the patient's preferences. Seventeen of 42 (40.5%) patients preferred a collaborative approach to decision-making, but for five of 42 (11.9%) patients it felt like a patient-controlled choice, and for four it felt like a physician-controlled one.

Table 3. CPS: Patient's preferred and perceived involvement in SDM and concordance with surgeon's perspective

CPS items	Preference of the patient N=36	How it went according to the patient N=34*	What the surgeon thinks the patient prefers N=36	What the surgeon prefers N=36
Patient-controlled	8 (22.2%)	13 (38.2%)	13 (36.1%)	13 (36.1%)
Collaborative	17 (47.2%)	8 (23.6%)	15 (41.7%)	16 (44.4%)
Physician-controlled	11 (30.6%)	13 (38.2%)	8 (22.2%)	7 (19.5%)

Note: *Missing data of two patients

Associations with HN surgeons' observed level of SDM
Consultation time (β0.019, 95% CI 0.004 – 0.034, p=0.013), and a higher OPTION-score of patients were positively correlated (β0.606, 95% CI 0.34 – 0.87, p<0.001) with HN surgeons' observed level of SDM. No other significant associations were found. Additionally, no characteristics of surgeons were included in the univariate linear regression analysis due to the small number of participating surgeons.

Discussion

Main findings

This study explored the current state of SDM in the complex setting of HN oncology. Although both surgeons and patients perceived a relatively high level of SDM, participation in SDM during consultation was observed to be lower than reported. Moreover, when looking at patient involvement, we found that both patients and surgeons mostly preferred a collaborative approach to the decision-making process. In almost two-thirds of the cases, surgeons' assumptions aligned with patients' preference for involvement. However, the mismatch in the remaining cases and the nine consultations that had not taken place as preferred by the patient demonstrate that discordance in surgeons' and patients' perceptions of decision-making roles is still commonly present. Furthermore, the duration of the consultation and patient OPTION-score were correlated with the observed SDM level of surgeons. No other associations were found.

Interpretations and comparing studies

Overall, surgeons in our study were observed to apply SDM moderately, with a median total OPTION-score of 48.0%. This finding was somewhat contrary to our expectations, as it indicates a somewhat higher level of SDM compared to what has been reported in other studies[33, 34, 39, 40, 53, 54]. One explanation for this higher OPTION-score may be that treatments for HNC are extensive and have a significant impact on patients' OoL, requiring a trade-off between survival and organ preservation through elaborate discussion[23, 55, 56]. Consequently, the higher score observed was primarily due to surgeons effectively discussing the (recommended) treatment option(s) (OPTION item 4). However, this tendency still reflects a common physician behavior that may hinder the full implementation of SDM, even if they express support for it[57]. It is important to note that the surgeons performed less well on those OPTION items (i.e., item 1 'goal talk', item 5 'decision talk', item 6 'integrative decision talk', and item 7 'evaluation talk') that specifically address SDM behavior, suggesting room for improvement in these areas.

Similar to surgeons, patients were observed to participate moderately in the decision-making process (median total OPTION-score 42%), scoring low on asking about alternative treatment options (OPTION item 2) but moderate on all other items. On the other hand, caregivers participated considerably less during consultations (median 24%), with median score indicating low participation across all OPTION items. While our primary focus was on the performance of surgeons and patients as key actors in the decision-making process, caregivers are often involved in patients' care. Although we did not delve into caregivers' contributions further in this study, exploring the dynamics

of the relationship between the patient and caregiver could provide valuable insights. Exploring this relationship could enhance our understanding of patient involvement, and future research could incorporate qualitative study designs to explore this aspect further[58].

When exploring both levels of SDM, a discrepancy appears to exist between surgeons' and patients' perception of SDM and the extent to which we observed SDM being employed. As expected, both surgeons and patients perceived SDM to be adequately implemented during consultation, which is consistent with previous research[33, 34, 38, 39, 53, 54], indicating that surgeons and patients tend to overestimate the extent of SDM in their consultations. This discrepancy between perception and observation may stem from a lack of complete understanding of what SDM truly involves, leading surgeons and patients to believe that SDM has occurred[59, 60]. Consequently, they might have misinterpreted aspects of counseling as SDM, whereas objective scoring may indicate otherwise. Additionally, they might have mistaken the mere inclusion of some SDM-related components, such as discussing patients' goals, values and preferences, with the quality of discussing them. Another explanation for this discrepancy may be that surgeons and patients reported on their overall satisfaction with the consultation rather than on the perceived level of SDM. However, given the complexity and potential impact of the treatment decisions, it is important to improve the decision-making process with HN patients, especially since SDM has been shown to be beneficial for various patient and healthcare-related outcomes[5-10]. As such, given the overall satisfaction of surgeons and patients with the current state of the decision-making process in HN oncology, we recommend future research to explore these considerations.

Furthermore, patients' preferences for involvement in decision-making vary widely, and discrepancies between the preferred and perceived level of involvement are often observed[14, 33, 53, 61]. In our study, the surgeons almost never explicitly asked the patient to what extent they wished to be involved in the decision-making. Similarly, we found this discordance in surgeons' assumptions of patients' preference for involvement in decision-making and patients' actual preference, with surgeons overestimating patients' preferences eight times and underestimating them five times. This highlights the need for more attention to patients' involvement preferences by HN surgeons, especially since discordance between preferred and actual involvement has been reported to substantially affect diverse patient outcomes, such as patient satisfaction, patients' understanding of information, fulfillment of information needs[62], and both physical and emotional QoL[63].

Lastly, a longer consultation time and a higher patient OPTION-score were found to positively increase surgeons' OPTION-score. Longer consultation time and an active patient during SDM are two known correlates[33, 38, 39]. However, further implementation and improvement of SDM into HNC decision-making does not necessarily have to lead to prolonged duration of the consultation[64, 65]. Although, consultation time may initially increase while healthcare providers are still in training and learning to apply SDM in their consultations, the duration of the consultations may decrease once they have acquired adequate SDM skills[66]. While we hypothesized that being an older patient and lower literacy would relate to a lower OPTION-score, as suggested in qualitative research[67], we found no significant correlations for any patient and tumor characteristic.

Limitations

We acknowledge that this study has some limitations. First, due to the exploratory nature of the study, only five surgeons from one hospital were included. Nevertheless, an attempt was made to assemble a reality-based group, with different ages and only one female surgeon (out of 2 employed). Multivariate analysis was not possible due to limited power, indicating the need for more research on SDM in HN oncology. Second, consultations were only audio recorded, whereas videos could have provided more insight into the communication process through nonverbal communication[68]. Third, surgeons' effort to apply SDM may have been stimulated by our study, as they were aware of being audiotaped. However, effect of the presence of an audio recorder during consultation has been reported to be negligible[69]. Fourth, the proposed treatment modality may have influenced the duration of consultations. For instance, HN may spend less time explaining radiotherapy treatment plans in detail compared to surgical procedures. This suggests that rather than the consultation length itself being directly related to SDM, the type of treatment proposed might influence the length of the consultation. Fifth, the SDM-Q9 and SDM-Doc questionnaires seem to be overly generic instruments for measuring perceived SDM levels. They lack detailed elaboration of each item, which is necessary to fully appreciate the quality of SDM. Lastly, although the OPTION^{mcc+} reflects the three-talk model of SDM, it cannot be directly compared with the SDM-Q-9 and SDM-Q-DOC questionnaires due to the difference in items. For example, OPTION items 1 'goal talk', 3 'team talk', 6 'integrative decision talk', and 7 'evaluation talk' do not appear to be exactly included in the SDM-Q questionnaires. No statistical correlation exists between all items of both measures that assess the same part of the SDM process[70]. Measuring SDM thus so far remains challenging, making the need for future research using measures with the exact same items that are comparable even more profound.

Conclusion

This exploratory study revealed that SDM in HN oncology of a tertiary hospital in the Netherlands is being applied to a moderate extent. However, a significant gap exists in the discussion of patients' values, goals, and preferences, indicating that more attention and involvement from healthcare providers is required. It is therefore essential to raise awareness about what SDM truly entails, especially considering the high prevalence of decisional conflict and regret, that both surgeons and patients tend to overestimate the extent of SDM compared to objective observations, and different perceptions on patient involvement exist. Moving forward, future research in the context of HN oncology should delve deeper into investigating the duration of consultation and patient OPTION-score, as they appear to be associated with a higher objective physician SDM-score. Specifically, exploring how SDM can be implemented without extending the consultation time may contribute to facilitating SDM uptake. Additionally, it is important to explore methods for effectively assessing both observed and perceived SDM levels in clinical practice. Enhancing SDM in HN oncology could lead to better patient and healthcare-related outcomes. As such, addressing the identified gaps in SDM practice is needed for improving patient care and healthcare delivery in this setting.

Practice implications

Our study offers insight to SDM in HN oncology and presents opportunities for improvement. Although it appears that the majority of patients and surgeons prefer to make the final treatment decision together, we believe that it is the healthcare provider's responsibility to take the lead in supporting the patient in decision-making, particularly in such stressful situations as HN oncology. This involves assessing the patients' values, needs, and preferences, taking into account the most relevant clinical evidence available, before making a joint decision about the course of action. Therefore, we suggest that healthcare providers ask as many open (follow-up) questions when discussing patient's values, needs, and preferences and listen carefully to gain more insight into their patients' lives, what is important to them, and what doubts, concerns and fears they may have. This is important, as patients' goals, values, and preferences regarding different treatment options, as well as rounding off the decision-making process during consultations, appeared to require improvement.

Furthermore, education and awareness campaigns have recently been launched that highlight the importance and benefits of SDM[71]. Nevertheless, whilst the concept of SDM has increasingly found its way into medicine and is also included in the vision document for Dutch medical specialists[72], HN surgeons tend to overestimate how skilled

they are at applying it. We therefore recommend for communication skills training in medical (follow-up) training programs in SDM. This training should be part of the Continuous Medical Education (CME) program to keep the SDM skills of surgeons' up-to-date[73-77]. Lastly, the use of additional resources, such as decision aids, audiovisuals, and written materials, might be helpful in implementing SDM as they allow patients to process information through various channels[78-80].

Appendix A. SDM-Q-9 and SDM-Q-Doc items

Item	Description	Referred to in the text
Item 1	Clarifying a decision needs to be made	'clarification'
Item 2	Eliciting the patients' preferred involvement	'involvement'
Item 3	Stating there is more than one way to deal with the problem	'alternatives'
Item 4	Explaining the pros and cons of treatment options	'options'
Item 5	Investigating if the patient has understood all the information	'understanding'
Item 6	Identifying the patients' preferred treatment option	'preference'
Item 7	Weighing the treatment options	'weighing'
Item 8	Making a shared decision	'decision'
Item 9	Agreement on follow-up arrangements	'agreement'

Appendix B. OPTION^{mcc+} items and measure scoring guide

Item	Behavior description
1	Goal talk: identify patient values and goals of care
2	Alternative option talk: discussion of alternate options
3	Team talk: forming a partnership
4	Option talk: information about options
5	Decision talk: eliciting patient's preferences
6	Integrative decision talk: integrating patient's preferences
7	Evaluation talk: check satisfaction with choice and SDM process

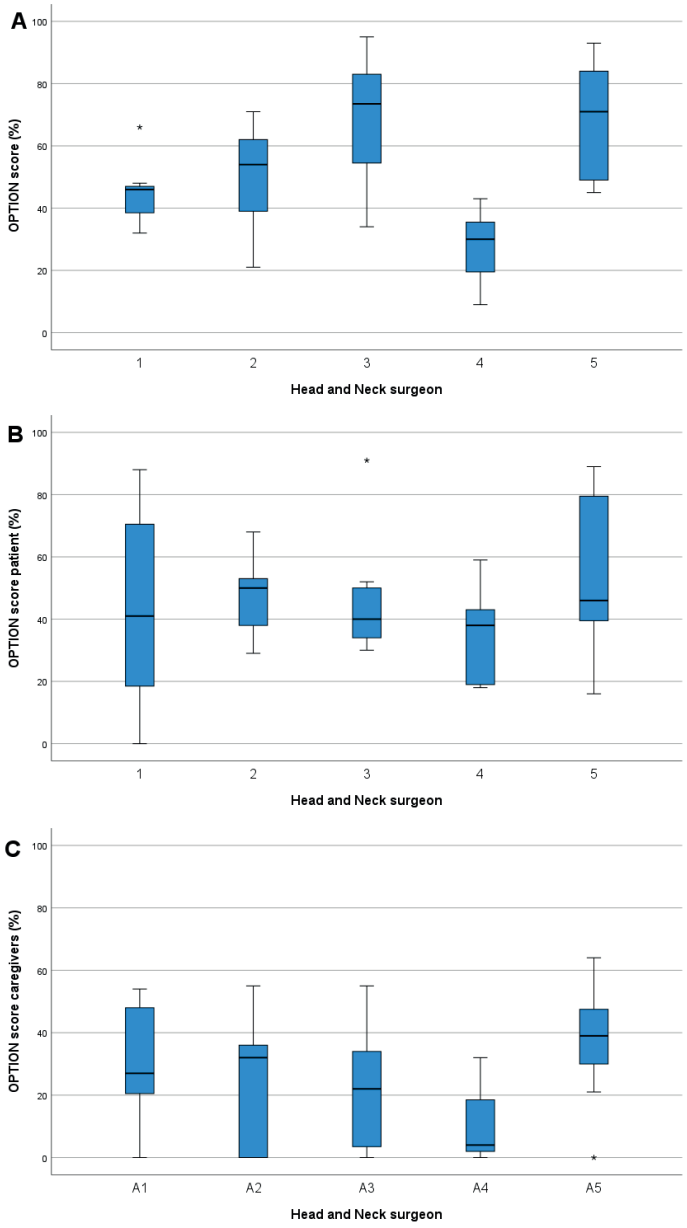
Score for physicians	Description (based on the OPTION^{mcc})
0 = no effort	Zero effort was observed. The behavior is not observed.
1 = minimal effort	Efforts to communicate could be implied or interpreted. A minimal attempt is made to exhibit the behavior.
2 = moderate effort	Basic phrases or sentences used. The behavior is exhibited to a good standard.
3 = skilled effort	Substantive phrases or sentences are used. The behavior is exhibited to a good standard.
4 = exemplary effort	Clear, accurate communication methods are used. The behavior is executed to a very high standard.

Appendix B. Continued

Score for patients and relatives	Description (adapted based on OPTION^{mcc} manual)
0 = passive	No, or minimal participation (e.g., only "yes", "no" or "uhu"
1 = responsive	Answers concisely on questions (short/one sentence answers, or short responses to the doctor, e.g., 'What?')
2 = very responsive	Answers in detail on questions (multiple or long sentences as answers or questions in response to the doctor, e.g., 'So you mean that X?'
3 = active	Answers and asks questions (more than one question(s) that add new information to what is already discussed)
4 = very active	Answers and asks questions, brings in own ideas, and shares perceptions

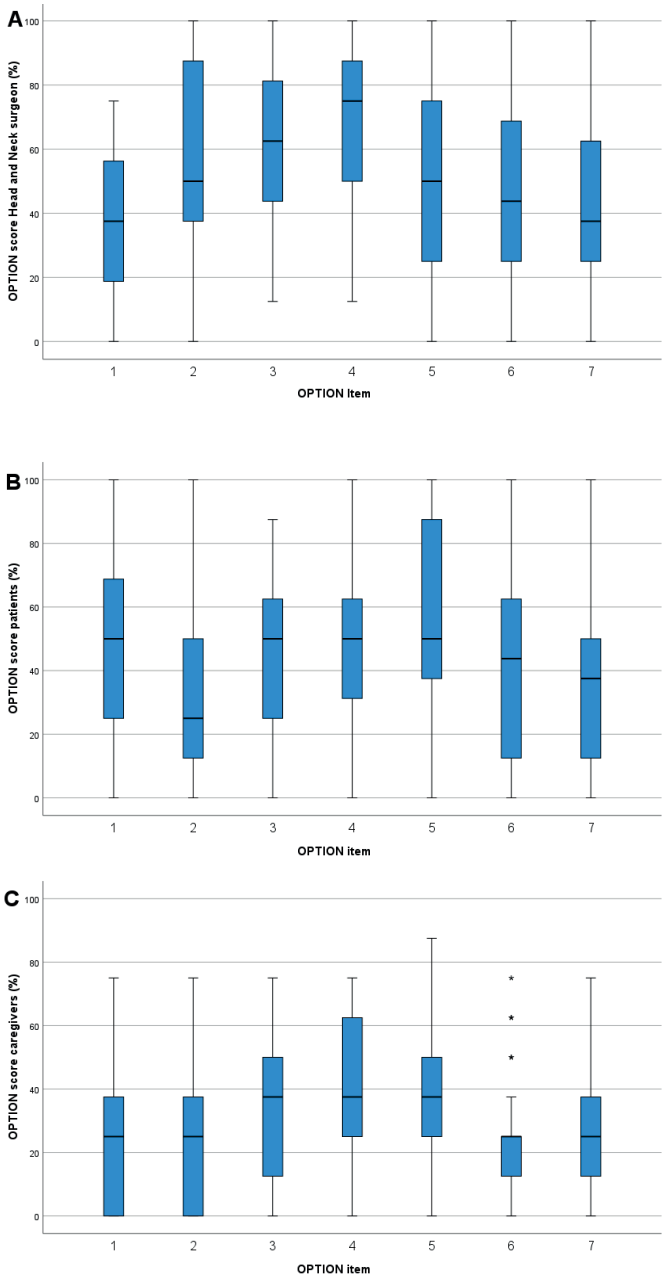
Appendix C. Observed and perceived level of SDM per head and neck surgeon

Surgeon	OPTION-score Median (range)	SDM-Q-Doc Median (range)	SDM-Q-9 Median (range)
1	46.0% (32.0-66.0%)	57.8% (46.7-91.1%)	93.3% (55.6-100.0%)
2	54.0% (21.0-71.0%)	80.0% (26.7-84.4%)	51.1% (11.1-100.0%)
3	73,5% (34.0-95.0%)	72.2% (55.6-80.0%)	80.0% (37.8-95.6%)
4	30.0% (9.0-43.0%)	82.2% (66.7-86.7%)	77.8% (20.0-100.0%)
5	71.05% (45.0-93.0%)	71.1% (57.8-80.0%)	68.9% (8.9-100.0%)



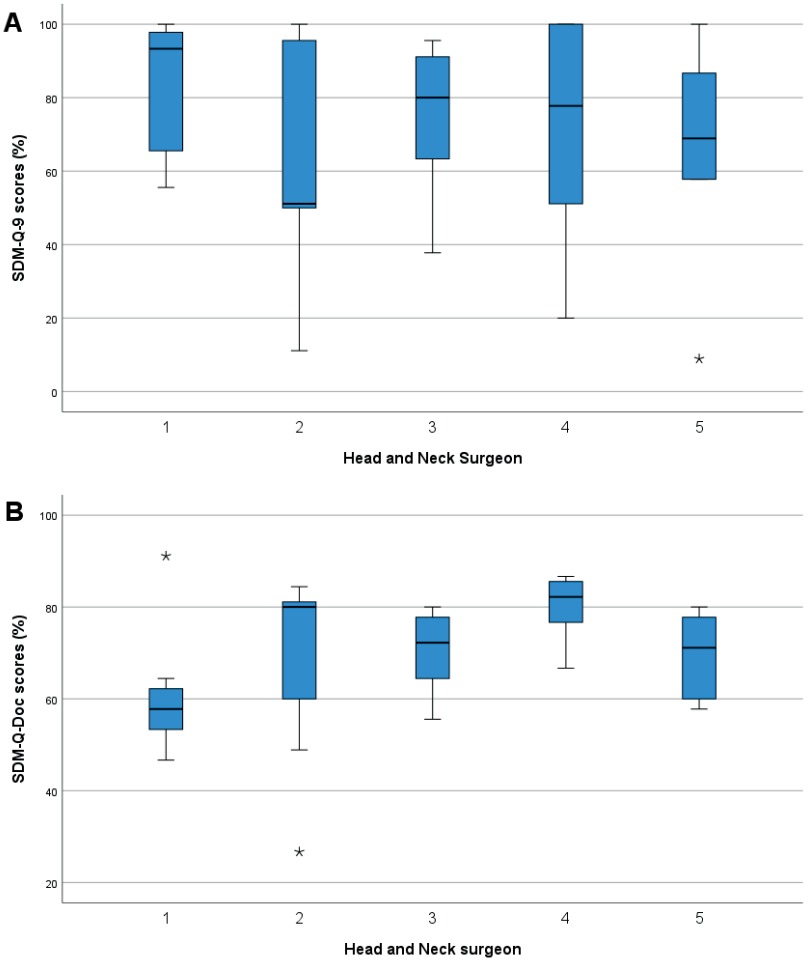
Appendix D. OPTION^{mcc+} scores per head and neck surgeon

Note: (A) Rescaled total OPTION score physician per head and neck surgeon. (B) Rescaled total OPTION score patients per head and neck surgeon. (C) Rescaled OPTION score relatives per head and neck surgeon. Boxes represent values between the 25th and 75th percentiles, whiskers the upper and lower adjacent values, and the horizontal lines represent the median values. Outliers are displayed as asterisks.



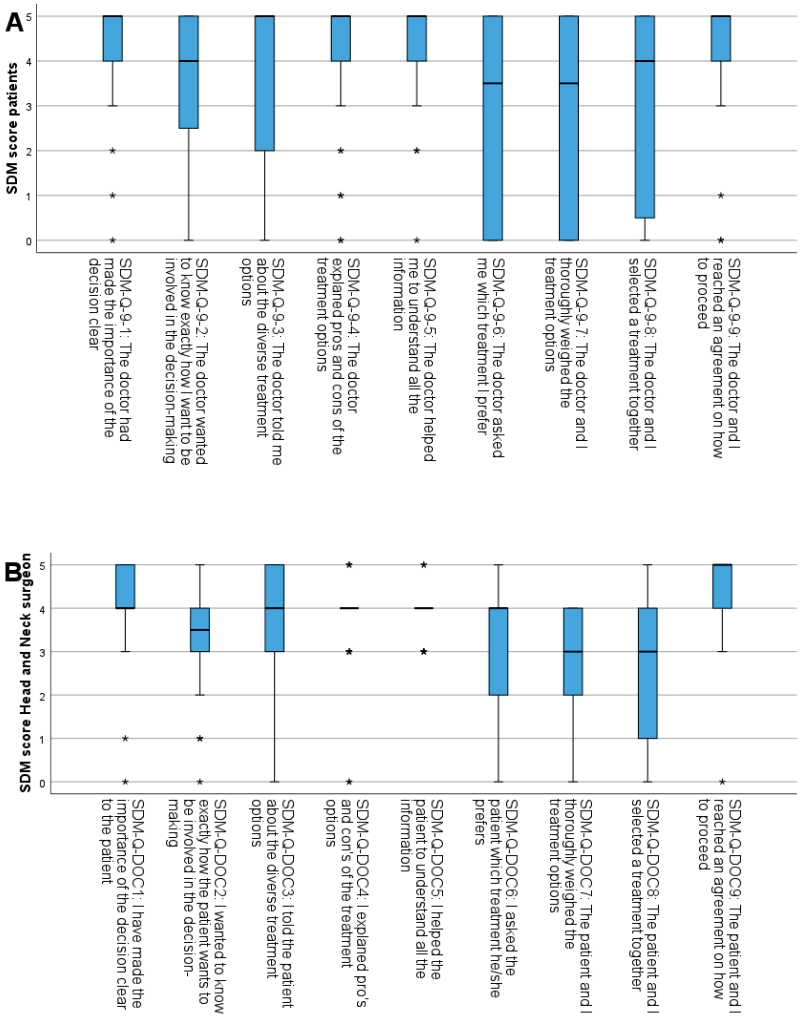
Appendix E. OPTION-scores per item

Note: (A) Physicians' OPTION scores for each of the 7 items. (B) Patients' OPTION scores for each of the 7 items. (C) Relatives' OPTION scores for each of the 7 items. Boxes represent values betweent he 25th and 75th percentiles, whiskers the upper and lower adjacent values, and the horizontal lines represent the median values. Outliers are displayed as astrisks.



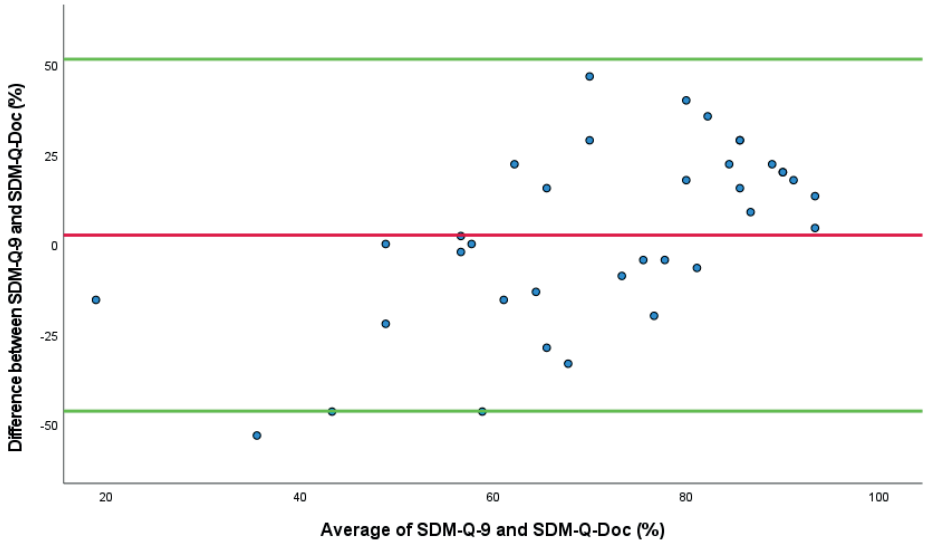
Appendix F. SDM-Q-9 scores and SDM-Q-Doc scores per head and neck surgeon.

Note. (A) SDM-Q-9 scores (patient) per head and neck surgeon. (B) SDM-Q-Doc scores per head and neck surgeon. Boxes represent values between the 25th and 75th percentiles, whiskers the upper and lower adjacent values, and the horizontal lines represent the median values. Outliers are displayed as asterisks.



Appendix G. SDM-Q-9 and SDM-Q-Doc scores per item

Note. (A) SDM-Q-9 scores (patient) per head and neck surgeon. (B) SDM-Q-Doc scores per head and neck surgeon. Boxes represent values between the 25th and 75th percentiles, whiskers the upper and lower adjacent values, and the horizontal lines represent the median values. Outliers are displayed as asterisks.



Appendix H. Bland-Altman plot for SDM-Q-9 and SDM-Q-Doc scores

Note: Bland-Altman plot of the differences between SDM-Q-9 (patient) and SDM-Q-Doc (surgeons) scores. The green horizontal line indicates the mean difference, and the red horizontal line the 95% limits of agreement ($p < 0.05$).

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Chapter 4

Decisional Conflict in Patients with Advanced Laryngeal Carcinoma – A Multicenter Study

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Abstract

Objectives: Decision-making for patients with a locally advanced laryngeal carcinoma (T3 and T4) is challenging due to the treatment choice between organ preservation and laryngectomy, both with different and high impact on function and quality of life (QoL). The complexity of these treatment decisions and their possible consequences might lead to decisional conflict (DC). This study aimed to explore the level of DC in locally advanced laryngeal carcinoma patients facing curative decision-making, and to identify possible associated factors.

Methods: In this multicenter prospective cohort study, participants completed questionnaires on DC, level of shared decision-making (SDM), and a knowledge test directly after counseling and six months after treatment. Descriptive statistics and Spearman correlation tests were used to analyze the data.

Results: Directly after counseling, almost all participants (44/45; 98%) experienced Clinically Significant DC score (CSDC > 25, scale 0-100). On average, patients scored 47% (SD 20%) correct on the knowledge test. Questions related to radiotherapy were answered best (69%, SD 29%), whilst only 35% (SD 29%) of the questions related to laryngectomy were answered correctly. Patients' perceived level of SDM (scale 0-100) was 70 (mean, SD 16.2), and for physicians this was 70 (SD 1.7).

Conclusion: Most patients with advanced larynx cancer experience high levels of DC. Low knowledge levels regarding treatment aspects indicate a need for better patient counseling.

Keywords: Laryngectomy, decision-making, decisional conflict, counseling, larynx cancer

Level of Evidence: Level IV

Introduction

Decision-making for patients with locally advanced laryngeal carcinoma (T3 and T4) can be challenging. Whereas historically these patients were treated with a total laryngectomy (TL)[1], larynx preservation became more popular over the years for trying to avoid permanent tracheostomy and loss of natural voice[2]. In selected cases, concurrent chemoradiotherapy (CRT) and radiotherapy (RT) have been proven to yield almost similar survival rates whilst sparing the larynx[3]. Only in very advanced tumors, several retrospective studies have shown that upfront laryngectomy probably has a survival advantage[4]. However, larynx preservation does not always lead to function preservation and can have significant long-term morbidity[5]. Research has shown that global quality of life (QoL) does not differ between patients who received larynx preservation treatments or TL, however, functionality does; TL patients have more speech-related problems, while CRT patients experience more swallowing-related problems[6,7]. For some patients with limited T3 primaries partial laryngectomies can be an alternative, although this modality is relatively rarely used in the Netherlands.

After TL, patients often experience social and adaptation problems, and associated distress. Therefore, They are sometimes willing to tradeoff survival percentages to preserve their larynx[2,8,9]. However, when choosing CRT or RT, patients and physicians should keep in mind that these treatments might fail. The potential risk of the need for a salvage TL (STL) after (C)RT failure is reported to be 16% for patients treated with concurrent CRT, and 31% for RT[10–12]. Compared to upfront TL, STL is associated with higher complication rates [13,14]. Therefore, decision-making on initial primary treatment is crucial, preferably through a shared decision-making approach, to enhance patients' knowledge, values and preferences[15].

The complexity of these treatment modalities and their possible consequences might lead to decisional conflict (DC). DC is defined as a state of uncertainty and difficulty experienced by an individual about the course of action to take[16]. The risk of DC is increased when patients have to weigh the pros and cons of multiple options, have inadequate knowledge, unclear personal values, and a perceived lack of support[17,18]. DC can lead to a range of negative consequences, such as postponed decision-making, selection of treatments misaligned with patient preferences, decisional regret and depression[19,20].

There is limited research on DC in head-and-neck cancer and specifically advanced laryngeal cancer. We therefore aimed to explore the level of DC, using a validated DC scale (DCS) in patients with locally advanced laryngeal cancer who are facing decision-making for treatment with the intent to cure. Additionally, we aimed to identify factors associated with DC.

Materials and Methods

Study sample and design

We conducted a multicenter prospective before-after design study (ClinicalTrials.gov Identifier: NCT03292341), investigating the impact of an online patient decision aid for advanced laryngeal cancer patients facing curative treatment decisions[21]. Here we describe the data of the usual care arm (the "before" arm).

Six Dutch head and neck centers participated in this study (Netherlands Cancer Institute, MAASTRO Clinic, University Medical Center Utrecht, University Medical Center Groningen, Amsterdam University Medical Center, and Radboud University Medical Center). Data were collected between March 2016 and February 2023.

Patients were eligible for participation if they were ≥ 18 years of age, diagnosed with primary T3N0M0, T3N+M0, T4N0M0 or T4N+M0 larynx cancer, who were potential candidates for a total laryngectomy or (chemo)radiation, proficient in the Dutch language, and able and willing to sign informed consent. Exclusion criteria were: not having an actual treatment choice (due to contra-indications or other medical reasons), candidates for partial laryngectomy and recurrent disease.

Patients were included after being discussed in the multidisciplinary tumor board (MDT) and if they met the inclusion criteria. They were provided with full study details and had the possibility to ask questions about the study to the researcher.

Included patients all signed informed consent. Counseling was mostly done by the head and neck surgeon (Otorhinolaryngologist) (table 1) although most patients were also seen by a radiation oncologist and often a medical oncologist, even when treated surgically. After this counseling consultation, organized according to routine local protocol they received the baseline questionnaires (T1) about their tumor and the suggested treatment option. Their consulting physician also filled in a questionnaire (SDM-Q-Doc). Patients were invited to fill in the follow-up questionnaire (T2) six months after the end of treatment and disease-free (figure 1). The patient questionnaires at T1 and T2 were identical, with the only difference being that T2 did not again include the sociodemographic questionnaire. The questionnaires consisted of: Decisional Conflict Scale[16], SDM-Q-9[22], Control Preference Scale[23] and a study-specific knowledge test.

Figure 1. Workflow of the study

Measures

Sociodemographic and clinical characteristics

We collected data on the patients' age, sex, educational level, marital status, employment status, family history of head-and-neck cancer, comorbidities, diagnosis, tumor stage, tumor subsite, initial treatment, and adjuvant treatment.

Decisional Conflict Scale

Decisional conflict (DC) was measured with the validated Decisional Conflict Scale (DCS)[16,24]. This 16-item scale has five subscales: feeling informed, decisional uncertainty, clear values, support, and quality of decisions. Each item is scored on a five-point Likert scale from 0 (strongly agree) to 4 (strongly disagree). Total scores and subscale scores are calculated. Scores can range from 0 (no DC) to 100 (extremely high DC). DCS < 25 are associated with implementing decisions, while scores >37.5 are related to decision delay and uncertainty about the choice[16]. A score >25 was used as cutoff for Clinically Significant DC (CSDC). This cutoff point is most used to distinguish between normal scores and harmful levels of decisional conflict[25–27].

Shared Decision-Making

The Shared Decision Making (SDM) process was assessed with the Dutch versions of the SDM-Q9 instrument (for patients) and SDM-Q-Doc (for physicians), which have both been validated for this purpose[22,28,29]. The instruments provide nine statements, rated on a 6-point scale from 0 (completely disagree) to 5 (completely agree). Scores can range from 0 (no perceived SDM) to 100 (highest level of perceived SDM). There is no cutoff point for this questionnaire.

Control Preference Scale

The Control Preference Scale (CPS) is a validated questionnaire comprising 5 items and assesses patients' desire for involvement in decision making. The items are: *I prefer (1) to make the decision alone, (2) to make the decision alone, after considering the physicians' opinion, (3) to make the decision together with the physician, (4) the physician to make the decision after considering my opinion, (5) the physician to make the decision alone*[9].

Knowledge Test

A study-specific knowledge test was constructed to assess patients' knowledge after counseling. It used 20 statements on the different treatment options, which could be rated as "true", "not true" or "do not know". The knowledge test included eight questions on TL, five on RT and seven on CRT. Internal consistency was assessed using Cronbach's alpha, to ensure that the questionnaires' items consistently measured the same underlying construct. The number of correctly answered questions was divided by the total number and multiplied by 100% to obtain a percentage of correctly answered questions. The same scoring was done for the subscores per treatment option and treatment group.

Statistical analyses

All statistical analyses were performed with IBM SPSS Statistics for Windows, Version 27 (2020; Armonk, NY: IBM corp.). Descriptive statistics were used to summarize the samples' characteristics and describe the levels of DC. Spearman correlations were performed to explore which variables are associated with DC. Testing for differences over time (T1 and T2) were done with the appropriate test depending on type and distribution of the data. A Bland-Altman analysis was employed to assess the agreement and potential differences in responses to Shared Decision-Making (SDM) questionnaires between physicians and patients.

Ethics

This study was conducted according to the principles of the Declaration of Helsinki[30]. The study received approval from the Ethical Review Committee of the Netherlands Cancer Institute under registration number IRBd22-023, and each local medical ethics review board at participating centers also granted their approval.

Results

Participants

Of the 54 approached patients, 51 patients agreed to participate in this study. Reasons for not participating were stress of diagnosis (n=2) and no interest (n=1). Of those, 45 returned the informed consent form and questionnaire T1. Only twenty-six patients (58%) returned the questionnaires six months after treatment (T2): eight patients were deceased, six had transitioned to palliative care, four refused to continue participating, and one patient was lost to follow-up. Thirty-five physicians returned their questionnaires at T1, of which most were Head-and-Neck surgeons (80%).

Table 1 represents the patients' characteristics. The median age was 64.7 years. Most patients were male (76%), and the majority had a low educational level (54%). Only 18% of the patients were employed. Most laryngeal cancers were located in the supraglottic subsite (62%) and classified as T3N0 (47%). Seventeen patients were treated with a TL (38%), sixteen with RT-alone (36%) and eleven with CRT (27%).

Table 1. Patient characteristics

Patients (N=45)	**N (%)**
Age (years): Median, range	64.7, 48-91
***Sex**:*	
Male	34 (76)
Female	11 (24)
TN-classification*:	
T3N0	21 (47)
T3N+	5 (11)
T4N0	13 (29)
T4N+	6 (13)
Subsite:	
Supraglottic	28 (62)
Glottic	11 (24)
Transglottic	3 (7)
Subglottic	3 (7)
Treatment:	
RT	16 (36)
CRT (cis/cet)	12 (26)
TL + RT	14 (31)
TL	3 (7)

Table 1. Continued

Patients (N=45)	**N (%)**
***Educational level**:**	
Lower educational level	24 (53)
Intermediate educational level	18 (40)
Higher educational level	3 (7)
Employed:	
Yes	8 (18)
No	16 (36)
Sickness benefits law / Sickness insurance law	2 (4)
Retired	19 (42)
Family member dependent on income	
Yes	16 (36)
No	29 (64)
Counseling physician*	
Medical oncologist	1 (3)
Radiation oncologist	6 (17)
Head-and-Neck surgeon	28 (80)

Abbreviations: SD= Standard Deviation; N = sample size; TN = Tumor, Node; RT = radiotherapy; CRT = chemoradiation, cis = cisplatin; cet = cetuximab; TL = total laryngectomy.
**TN-classification; TN-classification was documented instead of TNM-classification (UICC version 8) since the presence of distant metastasis (M) was an exclusion criterion.*
*** Lower: Primary general and primary vocational education. Intermediate: Secondary vocational and general secondary education. Higher: Higher vocational and academic education*
**** Since not all physicians returned their questionnaires, the numbers add up to 35 (100%). We do not have access to the characteristics of the other physicians.*

Decisional Conflict

The median DCS after counseling was 73.44 (range 25-100). Almost all patients experienced CSDC (44/45, 97.8%). The median DCS six months after treatment was 73.44 (range 0-100), and 22/26 patients (84.6%) still experienced CSDC. A moderate positive correlation was observed between the baseline DC scores and the scores after treatment (Spearman r=0.589, p=0.002). As shown in figure 2, the patient with no CSDC at T1 maintained the same score at T2 (DCS=25). Three other patients did have CSDC at T1 (scores ranging 34.38-75.00) but did not at T2.

All five subscales (Uncertainty, Informed, Values Clarity, Support, and Effective Decision) had a median score of 75.00 at T1, with only the Uncertainty subscale decreasing to a median score of 66.67 at T2. There was no significant change in the DCS score (Mann-Whitney-U test, p= 0.405) and subscales over time (table 2).

Table 2: Decisional Conflict Scale and subscores at T1 and T2

	T1 Median (range)	T2 Median (range)	P-value*
DCS total	73.44 (25.00 - 100)	73.44 (0 - 100)	0.405
Uncertainty	75.00 (16.67 - 100)	66.67 (0 - 100)	0.154
Informed	75.00 (25.00 - 100)	75.00 (0 - 100)	0.405
Values clarity	75.00 (25.00 - 100)	75.00 (0 - 100)	0.426
Support	75.00 (8.33 - 100)	75.00 (0 - 100)	0.206
Effective decision	75.00 (6.25 - 100)	75.00 (0 - 100)	0.382
CSDC (>25)	44/45 patients (98%)	22/26 patients (85%)	0.137

*Abbreviations: T1, directly after counseling; T2, six months after treatment; DCS, Decisional Conflict Scale; CSDC, Clinically Significant Decisional Conflict (DCS > 25); *Mann-Whitney-U test*

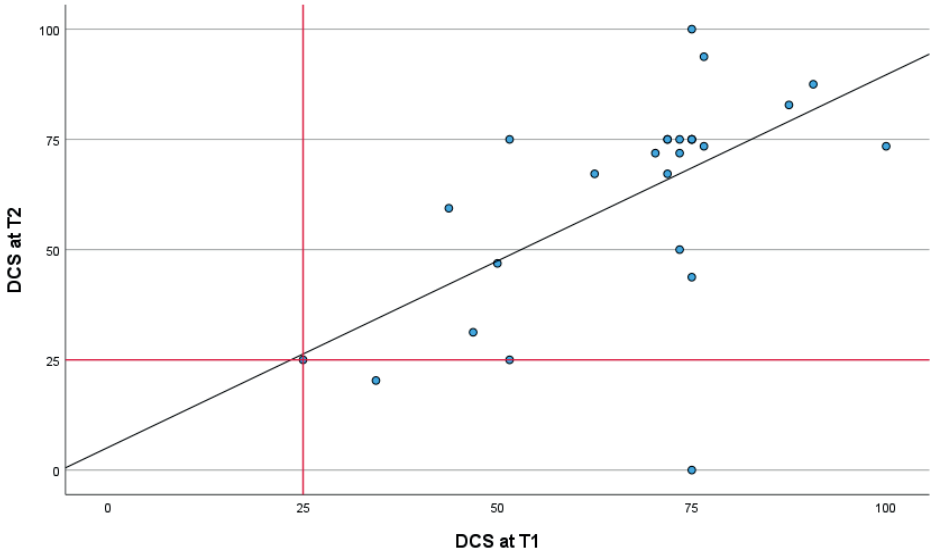

Figure 2. Scatterplot of DCS at baseline (T1) and after treatment (T2)

Only data for individuals who returned two DCS measurements are presented (N=26). The x-axis represents DCS scores post-counseling (T1), while the y-axis represents DCS scores six months post-treatment completion (T2). The red lines indicate the CSDC cutoff point (DCS>25 is CSDC), the black line is the total fit line.

Knowledge Test

The Cronbach's alpha was 0.807, indicating a high level of internal consistency among the items. At T1, patients on average answered 47.2% (SD 19.9%) of the questions on the knowledge test correctly. RT knowledge was best (69.4% correct, SD 28.8%), while TL knowledge was poorest (34.5% correct, SD 28.85%). Six months after treatment (T2), the mean total correctly answered questions slightly increased to 51.9% (SD 23.8%).

Regarding different treatment groups, TL patients had the highest median score for the overall number of correct answers (60%, range 20%-85%) and the CRT group the lowest overall score (median 43%, range 15%-85%). The lowest level on knowledge was seen on the questions regarding TL (range of medians 25-38%). See appendix A for all the results.

Shared Decision-Making

Patients' perceived level of SDM was 70.32 (mean, SD 16.22) at T1. Physicians scored a mean of 69.97 (SD 1.71). The mean difference between the SDM scores of patients and physicians was -0.272 (SD 21.53), but this difference was not significant (p=0.75).

Control Preference Scale

Most patients (34/45, 76%) preferred sharing responsibility with their treating physician (statement 2, 3 and 4). Ten patients (22%) wanted their physician to make the treatment choice (statement 5), and one patient (3%) preferred to make the final decision alone (statement 1). See table 3 for the statements and results.

At T2, more patients preferred a certain level of SDM during decision-making (23/25, 92%). The same patient still would have made the treatment choice on his own, and there was a decrease to one patient that would have left the choice to the treating physician. This difference in time points was not significant (p=0.07).

Spearman correlations DCS

The level of perceived SDM by patients and doctors was weakly positively correlated with DC, suggesting that more experienced SDM (higher scores on the SDM questionnaire) leads to more DC in this patient selection (see table 4). No other correlations were found.

Table 3. Control Preference Scale statements and data

CPS statements	**T1** (N=45)	**T2** (N=25)
1. I prefer to make the final decision about what treatment I will receive	3% (1)	4% (1)
2. I prefer to make the final selection of my treatment after seriously considering my doctor's opinion	13% (6)	16% (4)
3. I prefer that my doctor and I share responsibility for deciding which treatment is best for me	49% (22)	60% (15)
4. I prefer that my doctor makes the final decision about which treatment will be used, but seriously considers my opinion	13% (6)	16% (4)
5. I prefer to leave all decisions regarding my treatment to my doctor	22% (10)	4% (1)

Table 4. Spearman correlations for the Decisional Conflict Scale

Variable	**Spearman correlation (95% CI)**	**P-value**
SDM		
Patient	0.290 (0.033 – 1.000)	**0.031**
Doctor	0.333 (0.053 – 1.000)	**0.025**
Score on knowledge test	-0.157 (-1.000 – 0.095)	0.152
Control Preference Scale	-0.037 (-1.000 – 0.211)	0.405
Tumor stage	0.120 (-0.132 – 1.000)	0.217
Tumor subsite	-0.109 (-1.000 – 0.142)	0.237
Treatment	0.018 (-0.229 – 1.000)	0.453
Age	-0.006 (-1.000 – 0.241)	0.486
Sex	0.038 (-0.210 – 1.000)	0.402
Educational level	-0.107 (-1.000 – 0.144)	0.242

Discussion

Our study found that almost all patients with locally advanced laryngeal cancer experienced clinically significant decisional conflict (CSDC, 97.8%). The median DCS score (73.44) was alarmingly high during the decision-making process (T1) and remained high for most patients over time (T2). The DCS subscale analyses showed similar patterns with no significant changes over time.

To our knowledge, only one study reported on DC in laryngeal cancer patients and showed a mean DCS score of 25.6 (range 0-78)[31], which is much lower than our findings. However, they included all tumor stages of which only nineteen patients (38%) had locally advanced laryngeal cancer. Recent research showed that almost half (48%) of the head-and-neck cancer patients faced CSDC[32]. A mix of head-and-neck cancer subsites and stages was included in that study, making it hard to compare with our data. They did not find significant predictors for CSDC in their univariate analysis but did not gather information regarding SDM. In contrast, our study included a homogenous group of patients, which may provide a more realistic image of the DC in patients with locally advanced laryngeal cancer who consequently face more complicated treatment decisions.

When comparing the DC scores and incidence of CSDC in other diseases, it can be concluded that both are remarkably high in our patient group. In comparison, women with breast cancer considering breast reconstruction experience a mean DCS score of 46.18 (SD 15.22) with 68% experiencing CSDC[33] and in men with localized prostate cancer a mean DCS-score of 37.3 (SD 18.1) was found[34].

Reasons for the high DCS scores in our group could be due to the high impact of all treatment options on quality of life, functional and aesthetic outcomes, and the potential risks. The information is complex and technical, and the tradeoffs between survival and larynx preservation are hard to interpret without sufficient knowledge. Risk factors for developing head-and-neck cancer are low social economic status (SES), low health literacy[35]. We did not investigate this in our sample, but this could contribute to the level of DC[36]. The decision on which treatment to choose is tough, even for the treating physician, and it requires careful consideration of many factors and weighing potential outcomes based on risk assessments.

The consequences of these high DC scores are not investigated in this study. But other research has shown that scores >37.5 are associated with fretting regularly, postponed decision-making and nervousness[19,27]. These could lead to a decline in QoL and decision regret. What we do know about our patient group is that they are at high risk

for depression and anxiety after treatment, which one could hypothesize might be partially caused by their high level of decisional conflict and low knowledge levels[37,38]. More research is needed to investigate the consequences of CSDC for this patient group.

A weak but significant positive correlation was found between the perceived level of SDM by physicians and patients, and DC, whereby experiencing more SDM resulted in a higher DC score. This finding is in contrast with other research, where experiencing more SDM has been correlated with experiencing less DC[39–41]. These relationships could be population-specific, and the disparity may be due to the very complex information HNC patients receive and their relatively low educational level, making the shared information hard to process. If this is indeed the case, this suggests that current shared decision-making is insufficiently tailored to the capabilities of this patient group. Furthermore, it is essential to note that SDM questionnaires are inherently subjective and might not accurately reflect the extent to which there was SDM, thus introducing uncertainty regarding whether SDM was effectively applied[42,43]. One should keep in mind that this is a relatively small sample for correlation analysis, with a high number of CSDC and high scores on the SDM questionnaires, which limits the possibility of finding precise correlations. Hence, these findings should be cautiously interpreted.

A French study investigating the personal treatment preferences of otolaryngologists/head-and-neck surgeons[44] and radiation-oncologists[45] for advanced laryngeal cancer has demonstrated the challenge of decision-making among physicians. Their findings revealed that physicians' personal choices were almost evenly split between TL and larynx preservation. The proportion of potential cure they were willing to give up to preserve their larynx was relatively low (median 15%, range 5-100%). A small minority (4.2%) expressed a willingness to give up any chance of cure to avoid TL entirely. Interestingly, they found that specialists regularly attending the head-and-neck oncology tumor board, and specialists with more years of practice were more likely to consider a higher survival tradeoff to preserve their larynx. These results underscore that even with substantial knowledge and insights, the complexity of treatment options continues to pose significant challenges to the decision-making process.

In a study examining the treatment preferences of 309 individuals without cancer who were presented with a scenario of advanced laryngeal cancer, it was found that 40 out of 309 (12.9%) were unable to make a treatment choice[2]. Notably, almost 25% of the patients were unwilling to make any compromise on achieving a cure to preserve their larynx. The extent of cure that patients were willing to sacrifice varied widely, with an average of 33% and a range of 5-100%. This highlights the critical importance of eliciting and incorporating patients' values and preferences in decision-making.

Surprisingly low scores were found on the treatment knowledge tests. Patients answered less than half of the questions correctly. RT questions were answered most accurately, followed by CRT, and the lowest scores for TL. These results highlight the need for better education, counseling, and interventions to enhance patients' understanding, particularly regarding TL. Improving patients' knowledge could facilitate a more informed decision-making process, which is key for shared decision-making. Patient Decision Aids (PDA) are effective tools to improve patient knowledge and reduce DC[46,47]. Awareness of these high levels of CSDC might motivate physicians to pay extra attention to their counseling, especially in increasing patients' involvement and focusing on their preferences and values in life. Though it is hard to implement all these factors during counseling, proper training and using PDAs can contribute to higher knowledge levels, more engagement and hopefully a reduction in DC. The results of the impact of our PDA for locally advanced laryngeal cancer patients will follow in near future[21].

Limitations

Since this data is part of a more extensive study, this study was not powered for specific hypothesized correlations. Secondly, SDM questionnaires are subjective and have shown to overestimate the objectively performed SDM[42,43]. So these SDM data should be interpreted cautiously, and a more objective measure would be helpful to obtain a more reliable SDM outcome. Thirdly, only 26 patients (57.8%) handed in the questionnaires six months after treatment (T2), making it hard to draw conclusions on changes over time.

Conclusion

Most patients (>97.8%) with advanced laryngeal carcinoma face significant decisional conflict after counseling and after finishing treatment. They might be at risk for developing decision regret, depression and a lower quality of life, but this needs to be addressed in future research.

The perceived level of shared decision-making by patients and physicians was high. There were relatively low knowledge levels regarding treatment and the consequences, especially for total laryngectomy. These findings highlight the complexity of decision-making in patients with advanced laryngeal carcinoma and the need for interventions to reduce decisional conflict and improve knowledge levels.

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Chapter 5

The Impact of a Patient Decision Aid for Patients with Advanced Laryngeal Carcinoma – A Multicenter Study

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Abstract

Purpose: Patients with advanced larynx cancer face challenging treatment decisions. To address this, we developed and tested a patient decision aid (PDA), aiming to reduce decisional conflict (DC), and enhance knowledge and perceived shared decision-making (SDM).

Methods: In this multicenter study (ClinicalTrials.gov ID: NCT03292341, 2016-2023), a pre/post study design was used. Participants, meeting the inclusion criteria of advanced larynx cancer without distant metastasis, completed questionnaires on knowledge, DC and SDM immediately after counseling (T1) and 6 months post-treatment (T2). The intervention arm utilized the PDA (see https://beslissamen.nl/pda_launch.html?pda=tools/pda_larynx_en/story.html) before completing T1 questionnaires, while the usual care arm followed standard procedures. Between-group differences in outcomes were estimated using regression models with correction for case mix differences.

Results: Total DC score was significantly lower in the intervention arm (n=46) compared to the usual care arm (n=45) (adjusted mean difference -32, 95% CI: -37.4 ; -26.1, p<0.001). The intervention group demonstrated significantly higher overall knowledge (mean 69% correct) than the control group (mean 47% correct)(adjusted mean difference 24, 95% CI 15.3 ; 33.1, p<0.001). Almost all patients in usual care (44/45, 98%) experienced clinically significant DC (CSDC, DCS > 25), compared to 89% (41/46) in the intervention arm (adjusted OR 0.25, 95%CI 0.01; 1.9) p=0.238). Perceived SDM was significant higher in the intervention arm (mean 78.16) compared to the usual care arm (mean 70.32); however, both groups exhibited high levels.

Conclusion: The PDA for advanced laryngeal cancer effectively reduced decisional conflict, enhanced patients' knowledge and improved perceived SDM.

Introduction

The medical world has seen a gradual shift from paternalistic decision-making toward shared decision-making (SDM). This paradigm shift underscores the growing recognition of the patient's role in their healthcare journey, reflecting a broader trend across medical disciplines towards patient-centered care[1,2]. An effective way to improve the SDM process is the use of patient decision aids (PDA)[3]. PDAs are developed to enhance patients' knowledge by providing evidence based information on treatment options, risks, benefits, expected morbidity and possible outcomes[4]. Over the years, PDAs have demonstrated their utility by providing patients with a better understanding of treatment options and helping them articulate their personal preferences[3–5].

When dealing with advanced laryngeal cancer, a range of therapies is applicable, ranging from total laryngectomy (TL), concurrent chemoradiotherapy (CRT), or primary TL with postoperative (C)RT. Patients and doctors are therefore often confronted with challenging decisions[6–8]. Each of these treatments has a major impact on prognosis and quality of life, potentially affecting voice, appearance, breathing, smelling, taste, swallowing and eating[9–11]. The decision to undergo a voice-box removing total laryngectomy is extremely difficult, largely due to the enduring and significant permanent side-effects associated with such a procedure. Whilst larynx-preserving strategies offer an alternative, their oncological and functional success is not guaranteed, and failure may necessitate a salvage TL, which carries higher risks of complications than an upfront TL[7,12]. Hence, it is important to adequately inform patients about their primary treatment choice, taking patients' values and preferences into account[2].

The complexity of this choice may lead to decisional conflict (DC), a state of uncertainty about the choice to be made, aggravated by inadequate knowledge, unclear personal values and perceived lack of support[13–15]. DC can lead to a range of negative consequences, such as postponed decision-making, selection of treatments misaligned with patient preferences, decisional regret and depression[16,17].

Acknowledging these challenges, our research group developed a PDA specifically for patients with advanced laryngeal cancer[18], which was evaluated in a multicenter study. In our previous study evaluating the usual care, we showed that patients had low levels of knowledge regarding the possible treatments and experienced high levels of decisional conflict (DC)[19].

The objective of this study is to evaluate the impact of introducing our PDA as part of the decision-making process for patients with advanced larynx cancer, with a focus on its effect on decisional conflict, treatment knowledge, and the perceived level of shared decision-making. By doing so, we aim to contribute valuable insights into the optimization of patient-centered care in the context of advanced larynx cancer, addressing a critical gap in the existing literature.

Materials and Methods

Study sample and design

This is a multicenter study with a before-after design study (ClinicalTrials.gov Identifier: NCT03292341). The objective of the current study was to compare outcomes after implementation of the PDA to those in usual care. For data collection, the present study therefore utilized comparable methodology as the previously published study[19]. The sample size was based on an assumed decrease in decisional conflict with a standardized mean difference of 0.6, for which 45 patients per group were needed to achieve 80% power with an alpha of 0.05[20].

Patients were recruited in six Dutch head and neck centers between 2016-2023. Eligible patients were >18 years, diagnosed with of primary T3-T4 laryngeal cancer and Dutch proficient. Patients without choice in treatment due to medical conditions, or recurrent disease were excluded.

Patients meeting inclusion criteria were approached after the multidisciplinary tumor board (MDT) discussion. After signing informed consent, they received baseline questionnaires (T1) following their outcome interview. The physician (head and neck surgeon or radiation oncologist) simultaneously completed SDM-Q-Doc after consultation. The follow-up questionnaire (T2) was sent through mail, six months post-treatment (Figure 1).

The patient questionnaires for T1 and T2 included the Decisional Conflict Scale[15,21], SDM-Q-9[22–24], Control Preference Scale (CPS)[9], and a study-specific knowledge test. The T1 questionnaire contained additional personal situation questions (see supplements).

As this study follows a pre/post design, patients in the usual care arm were enrolled prior to PDA implementation, while subsequent patients were included in the intervention arm. For a visual representation, refer to Appendix A.

In the intervention arm, patients received extra information about the PDA and contact details of the main researcher (A.N.H.) for further queries. All patients were given a uniform instruction form outlining how to access the PDA website, including helpful tips like browser compatibility suggestions and the importance of enabling sound. Those without home computer access could use a consultation room computer, with the researcher nearby for assistance while ensuring privacy.

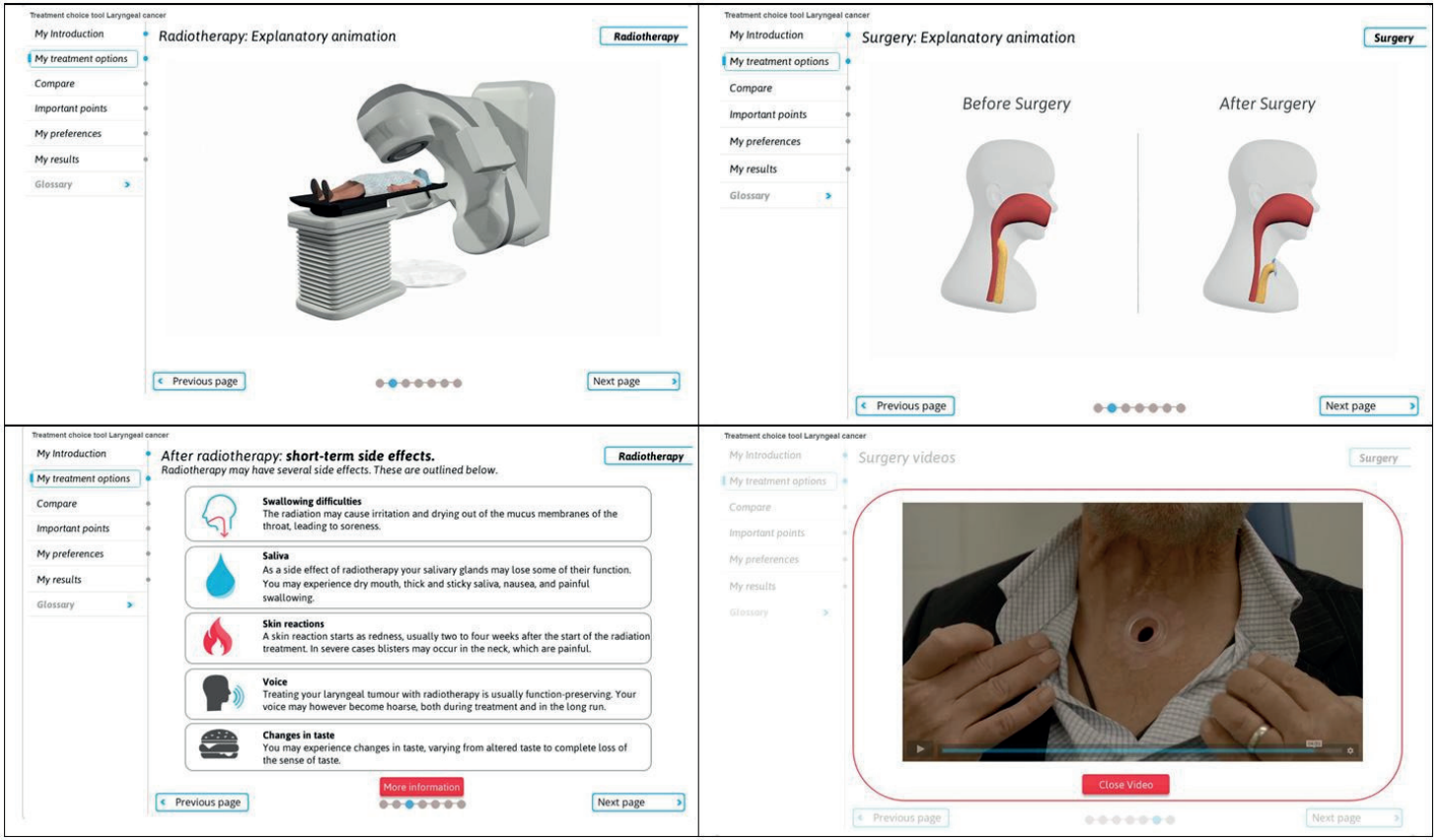

Figure 1. Overview of the PDA

The PDA

The PDA was developed by a team of head and neck surgeons, radiation oncologists, medical oncologists and a dedicated team of patients from two head and neck centers in The Netherlands in 2016[18], following the International Patient Decision Aid Standards (IPDAS) criteria[25,26]. After inclusion of usual care was completed, the PDA was published online in Dutch and English (www.beslissamen.nl).

Depending on age and TNM stage, patients would see different versions of the PDA depending on whether or not they would be candidates for the various treatment options, including RT, CRT and TL. Based on National Guidelines, chemotherapy was not offered above the age of 70 years[27]. Outcomes and their likelihood were based on a population-based study[28]. See figure 1 for an overview of the PDA.

Measures

Data on patient's age, educational level, marital status, employment status, family history of head-and-neck cancer, comorbidities, diagnosis, tumor stage, tumor subsite, treatment, adjuvant treatment, were gathered from hospital records.

The primary outcome Decisional conflict (DC) was measured with the validated Decisional Conflict Scale (DCS)[15,21]. As a secondary outcome, we compared Clinically Significant DC (CSDC), with a score >25 serving as the cutoff to distinguish between normal and harmful levels of decisional conflict[29–31]. Additional exploratory secondary outcomes included shared decision making (SDM), control preference and knowledge.

SDM was evaluated using validated Dutch versions of SDM-Q9 for patients and SDM-Q-Doc for physicians. Both instruments, with 9 statements each, use a 6-point scale (0 to 5), resulting in scores from 0 (lowest) to 100, wherein higher scores indicate better perceived SDM[22–24].

Additionally, patients' desire of involvement in decision making was assessed, using the Control Preference Scale (CPS) [9], for descriptive purposes.

A study specific knowledge test was conducted to investigate patients' knowledge after counseling. It used 20 statements on the different treatment options, which could be rated as "true", "not true" or "do not know". The number correct was used as the knowledge score.

Statistical analyses

All statistical analyses were performed with R version 4.3.3 in RStudio software. Descriptive statistics fitting the type and distribution of the data were calculated to summarize the characteristics of the sample. Between-group differences in patient and tumor characteristics were analyzed using chi-square tests, and an unpaired t-test for age.

Differences in total decisional conflict scores, knowledge and patient-experienced SDM were analyzed using linear regression. If assumptions of homoscedasticity and normal residual distributions were violated, we used bootstrapped 95% confidence intervals (b=1000). Differences in proportion of patients with CSDC, at baseline as well as 6-month follow-up, were analyzed using binary logistic regression. All regression models included propensity score correction to adjust for case-mix differences. The propensity score was calculated using a logistic regression model with arm as the dependent variable and Age, TNM, Subsite, and Education as independent variables. Treatment was not used in the PS correction since treatment choice was decided after counseling. Unpaired t-tests were applied to compare physicians' evaluation of SDM between usual care and intervention. A subgroup analysis of differences in knowledge between the control and intervention group was done using a Mann-Whitney U test. All secondary outcomes were considered exploratory and hence no multiple testing correction was applied.

Ethics

This study was conducted according to the principles of the Declaration of Helsinki[32]. The ethical review committee of the Maastricht University Medical Center assessed and approved this study (registration number IRBd22-023). Additionally, all other participating centers obtained approval from their respective Medical Ethics Review Committee.

Results

Participants

In total, 128 eligible patients were approached, of which 91 patients (usual care arm n=45, intervention arm n=46) were included and returned the informed consent and questionnaires (participation rate 71.1%).

Most patients were male, had a supraglottic tumor, a lower educational level, were retired and almost all had access to internet. Although there were no significant differences between the two study arms, there were some potentially clinically relevant differences. There were more advanced stages in the usual care arm, and the educational level was lower in the intervention arm. See table 1 for all characteristics.

Figure 2 shows the flow of patients through the study and reasons for loss to follow-up. N=35 and N=39 physician questionnaires were available for T1 and T2, respectively.

Decisional Conflict

Median total DC score in the usual care arm was 73.44 (range 0-100), in the intervention arm 35.94 (range (17.19-46.88). After correcting for minor case mix differences via propensity score correction, the adjusted mean difference was -32.3 (bootstrapped 95%CI: -37.4; -26.1, p<0.001). Significant lower DC was also seen in the total score of the DCS at T2, with an adjusted mean difference of -38.0 (bootstrapped 95%CI -50.1, -24.2, p <0.001). Table 2 lists total and subscale scores.

Almost all patients who participated in the usual care arm (44/45, 98%) experienced clinically significant DC (CSDC, *DCS > 25*), compared to 89% (41/46) in the intervention arm (adjusted OR 0.25, 95%CI 0.01; 1.9) p=0.238). Six months after treatment, 92% (23/25) of the patients in the usual care group still experienced CSDC, while in the intervention arm this 56.7% (17/30); adjusted OR 0.10 (95%CI 0.02 ; 0.44, p=0.005).

Knowledge Test

At T1, the intervention group exhibited significantly higher overall knowledge (median 75% correct) compared to the usual care group (median 45% correct). Knowledge is statistically significantly better in the intervention arm, with an average of 4.8 (95%CI 3.2, 6.6, P<0.001) percent point more correct.

At T2 we saw similar patterns, although not significant. Knowledge was higher in the intervention group with 6.4 percent point more correct (95%CI 1,2, 27.0, P=0.07)

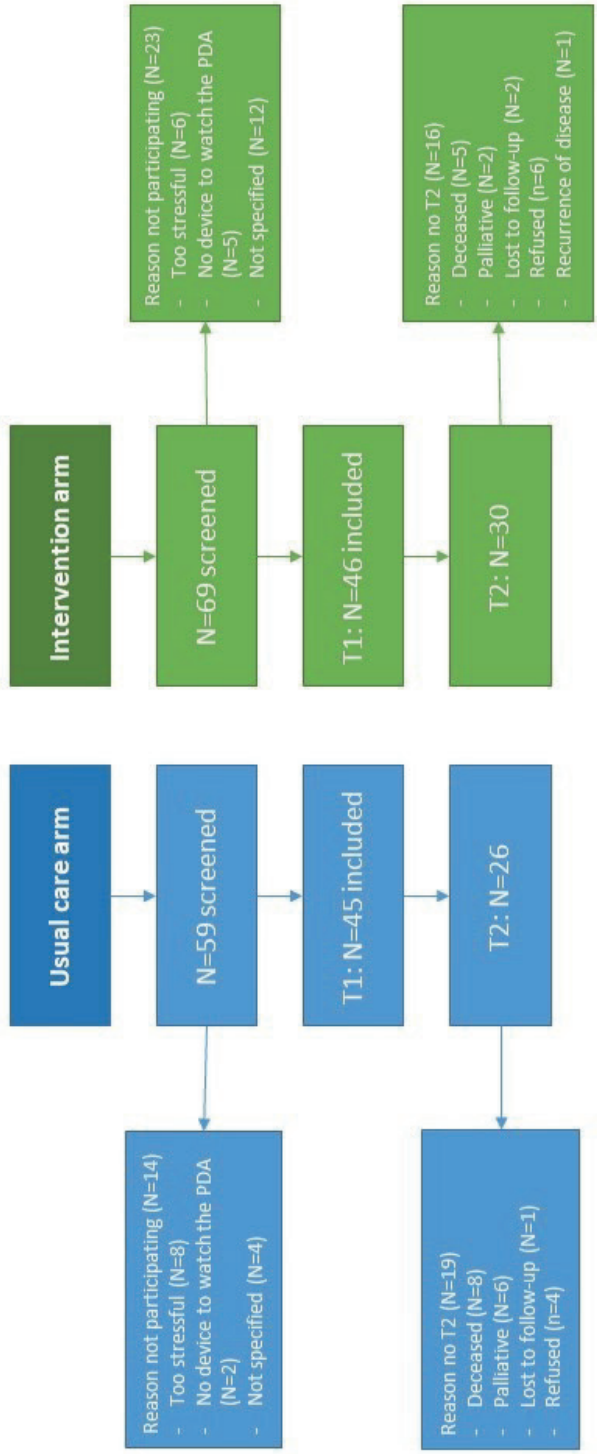

Figure 2. Flowchart of inclusions

Table 1. Characteristics of both study arms

Patients	Usual care (n=45) N (%)	Intervention (n=46) N (%)	p-value**
Age (years): Mean (SD), range	64.3 (9.8), 48-91	68.2 (10.8), 41-86	0.113
***Sex**:*			0.953
Male	34 (75.6)	35 (76.1)	
Female	11 (24.4)	11 (23.9)	
TN-classification*:			0.101
T3N0	21 (46.7)	22 (47.8)	
T3N+	5 (11.1)	13 (28.3)	
T4N0	13 (28.9)	6 (13)	
T4N+	6 (13.3)	5 (10.9)	
Subsite:			0.454
Supraglottic	28 (62.2)	29 (63)	
Glottic	11 (24.4)	15 (32.6)	
Transglottic	3 (6.7)	1 (2.2)	
Subglottic	3 (6.7)	1 (2.2)	
Educational level:			0.468
Lower educational level	24 (53.3)	39 (84.8)	
Intermediate educational level	18 (40)	7 (15.2)	
Higher educational level	3 (6.6)	0 (0)	
Occupational status:			0.229
Yes	8 (17.8)	6 (13)	
No	16 (35.6)	9 (19.6)	
Sickness benefits law / Sickness insurance law	2 (4.4)	2 (4.3)	
Retired	19 (42.2)	29 (63)	
Access to internet			0.689
Yes	39 (86.7)	41 (89.1)	
No	6 (13.3)	5 (10.9)	
Treatment received:			0.346
RT	16 (35.6)	24 (52.2)	
CRT (cis/cet)	12 (26.7)	10 (21.7)	
TL + RT	14 (31.1)	8 (17.4)	
TL	3 (6.7)	2 (4.3)	
Best supportive care	0 (0)	2 (4.3)	

Abbreviations: SD= Standard Deviation; N = sample size; TN = Tumor, Node; RT = radiotherapy; CRT = chemoradiation, cis = cisplatin; cet = cetuximab; TL = total laryngectomy.

**TN-classification; TN-classification was documented instead of TNM-classification since the presence of distant metastasis (M) was an exclusion criterium.*

***All testing was performed with chi-square, except an unpaired t-test for age*

Table 2: Decisional Conflict Scale and subscores at T1 and T2

Median (range)	Usual Care T1 N=45	Intervention T1 N=46	adjusted MD + 95%CI	P-value
DCS total	73.44 (25.00 - 100)	35.94 (17.19-46.88)	-32.3, -37.4; -26.1	**<0.001**
Uncertainty	75.00 (16.67 - 100)	41.67 (25-66.67)	-25.9, -33.0; -18.8	**<0.001**
Informed	75.00 (25.00 - 100)	33.33 (8.33-83.33)	-28.6, -36.9; -20.2	**<0.001**
Values clarity	75.00 (25.00 - 100)	33.33 (8.33-58.33)	-30.7, -37.5; -23.1	**<0.001**
Support	75.00 (8.33 - 100)	33.33 (16.67-58.33)	-36.9, -43.5; -28.1	**<0.001**
Effective decision	75.00 (6.25 - 100)	31.25 (12.5-50.00)	-38.6, -44.4; -32.2	**<0.001**

Abbreviations: T1, directly after counseling; T2, six months after treatment; DCS, Decisional Conflict Scale; CSDC, Clinically Significant Decisional Conflict (DCS >25) MD, Mean Difference

Knowledge was systematically better in all treatment subgroups, at both timepoints, after implementation of the PDA. TL questions had the lowest % correct, Radiotherapy (RT) questions had the highest % correct. (Table 3).

Shared decision-making

Patients' Perceived Shared Decision Making (SDM) was significantly higher in the intervention arm (mean 78.16, SD 8.31)) compared to the usual care arm (mean 70.32, SD 16.11) (p=0.005) with an adjusted mean difference of 6.2 (95% CI 0.4;12.0, p=0.006, with both arms exhibiting relatively high levels.

Six months post-treatment, perceived SDM level scores increased in both arms, with the intervention arm (mean 81.63, SD 10.39) remaining higher than the usual care arm (mean 71.88, SD 14.22, with an adjusted mean difference of 7.0 (95% CI -0.4; 14.4, p=0.0053). Physicians mean perceived SDM was 69.96 (SD 17.71), and no significant differences after introduction of the PDA (mean 68.21, SD 13.28). See appendix for B for all results.

Control Preferences

The majority of patients expressed a preference for collaborative decision-making, sharing responsibility with their treating physician, as indicated by statements 2, 3, and 4. This inclination was consistent in both study arms, with 76% (34/45) in the usual care arm and 87% (40/46) in the intervention arm (Table 4).

Usual care	Intervention		
T2 **N=25**	**T2** **N=30**	**adjusted MD + 95%CI**	**P-value**
73.44 (0 - 100)	25.00 (12.50-43.75)	-38.0, -50.1, -24.2	**<0.001**
66.67 (0 - 100)	25 (0-58.33)	-37.4, -49.4; -25.5	**<0.001**
75.00 (0 - 100)	25 (0-50)	-40.7, -52.7; -23.0	**<0.001**
75.00 (0 - 100)	25 (0-50)	-41.5, -53.2; -25.2	**<0.001**
75.00 (0 - 100)	29.17 (0-75)	-30.4, -44.0; -16.7	**<0.001**
75.00 (0 - 100)	25 (12.5-43.75)	-41.2, -51.8; -24.8	**<0.001**

Significant outcomes are displayed in bold.

Table 3. Results study specific knowledge test on treatment for different study groups

Patient groups Questions	**T1** N=45 Usual care	**T1** N=46 Inter-vention	**P-value**	**TL* (T1)** N=17 Usual Care	**TL* (T1)** N=10 Inter-vention	**P-value**
All treatments			**<0.001**			**0.035**
Median % (score 0-20)	45%	75%		60%	70%	
Range	(9)	(15)		(12)	(14)	
	15-85%	5-95%		20-85%	55-95%	
TL			**<0.001**			**0.002**
Median % (score 0-8)	25%	62.5%		25%	87.5%	
Range	(2)	(5)		(2)	(7)	
	0-100%	0-100%		0-100%	50-100%	
RT			**<0.001**			0.334
Median % (score 0-5)	80%	100%		60%	80%	
Range	(4)	(5)		(3)	(4)	
	0-100%	20-100%		0-100%	60-100%	
CRT			**0.002**			0.204
Median % (score 0-7)	42.9%	71.4%		43%	50%	
Range	(3)	(5)		(3)	(3.5)	
	0-100%	0-100%		0-100%	29-100%	

The usual care arm is represented in dark grey, while the intervention arm is shown in light grey The left column indicates the level of knowledge on treatments. The first row displays the groups, showing data for the entire group as well as data categorized based on the received treatment. Differences were assessed using the Mann-Whitney-U test.

	CRT (T1) N=12 Usual Care	**CRT** (T1) N=10 Inter-vention	**P-value**	**RT (T1)** N=16 Usual Care	**RT (T1)** N=24 Inter-vention	**P-value**	**T2** N=26 Usual care	**T2** N=30 Inter-vention	**P-value**
	45% (9) 20-75%	65% (13) 45-90%	**0.002**	43% (8.5) 15-85%	75% (15) 5-95%	**0.002**	55% (11) 5-85%	62.5% (12.5) 15-95%	0.136
	38% (3) 0-87.5%	56.3% (4.5) 0-87.5%	0.346	25% (2) 0-75%	56.3% (4.5) 0-100%	**0.002**	37.5% (3) 0-87.5%	62.5% (5) 0-100%	0.067
	80% (4) 20-100%	100% (5) 80-100%	**0.007**	80% (4) 0-100%	100% (5) 20-100%	**0.002**	80% (4) 20-100%	100% (5) 0-100%	**0.002**
	43% (3) 0-100%	85.7% (6) 43-100%	0.180	38% (2.5) 0-87.5%	71.4% (5) 0-100%	**0.044**	50% (3.5) 0-100%	57% (4) 0-100%	0.914

Significant p-values are highlighted in bold.*T1, directly after counseling; T2, six months after treatment; TL = Total Laryngectomy, RT = Radiation Therapy, CRT = Chemo Radiation Therapy.*
*This group also includes patients that received postoperative radiation therapy after TL

Table 4. Control Preference Scale statements and data

CPS statements	Usual Care T1 (N=45)	Intervention T1 (N=46)	Usual Care T2 (N=25)	Intervention T2 (N=30)
1. I prefer to make the final decision about what treatment I will receive	1, 2.2%	0, 0%	1, 4%	2, 6.7%
2. I prefer to make the final selection of my treatment after seriously considering my doctor's opinion	6, 13.3%	8, 17.4%	4, 16%	10, 33.3%
3. I prefer that my doctor and I share responsibility for deciding which treatment is best for me	22, 48.9%	22, 47.8%	15, 60%	13, 43.3%
4. I prefer that my doctor makes the final decision about which treatment will be used, but seriously considers my opinion	6, 13.3%	10, 21.7%	4, 16%	3, 10%
5. I prefer to leave all decisions regarding my treatment to my doctor	10, 22.2%	6, 13%	1, 4%	2, 6.7%

T1, directly after counseling; T2, six months after treatment;

Discussion

To our knowledge, this is the first prospective multicenter study evaluating the impact of a patient decision aid tool for patients with advanced laryngeal cancer. The results clearly indicate that introducing the PDA resulted in lower total DCS scores. Additionally, the intervention arm demonstrated significantly better knowledge about the possible treatments and scored significantly higher for perceived shared decision-making compared to patients receiving usual care. By providing comprehensive information and supporting patient involvement in the decision-making process, this PDA empowers patients with advanced laryngeal carcinoma to make informed decisions.

The observed significant reduction in total DC scores among participants who utilized the PDA was noteworthy and indicative for improvement in their decision-making process. However, reduction in mean DC resulted mostly from a narrower range, i.e., lower maximal scores, and despite this improvement, the proportion of patients with CSDC was not significantly different between the groups. This finding might be related to the choice of cut-off for CSDC.

In recent years, there has been an increased adoption of cut-off values for DC in clinical practice. Scores below 25 are often associated with the ability to implement a decision, whilst scores above 37.5 are indicative for decision delay. Consequently a threshold of ≥25/100 is most often defined a cutoff for CSDC[21]. These thresholds offer a quantitative framework for assessing the clinical relevance of DC. However, it's important to recognize that the utility of these cut-offs beyond their original context has not been extensively explored and for specifically life changing decisions in cancer treatment, different cutoff values might be clinically relevant[33].

Our study showed a significant difference in treatment knowledge between the intervention and usual care groups. Despite expectations that, after ending treatment, the knowledge gap would diminish, the difference in knowledge persisted at six months post-treatment. This underscores the enduring benefits of targeted educational interventions. Such interventions not only facilitate immediate comprehension but also support long-term coping with the outcomes of complex treatments like TL. The enhancement in perceived SDM levels within the intervention group aligns with our expectations. This improvement is probably due to the comprehensive nature and the audiovisual aspects of the information provided to these participants, covering all available treatment options. In contrast, the usual care group's knowledge and experience on the decision process largely depends on the specific information their

physicians choose to share. This variability can be attributed to individual doctors' preferences and their comfort level with SDM practices[4]. Furthermore they may not be aware of their shortcomings in facilitating an SDM approach, something we also saw in the high level of SDM scored by the physician, irrespective of the use of the PDA[34–36].

An interesting finding is the disparity in choosing non-surgical treatment between the intervention arm (78.2%, 36 patients) and the usual care arm (62.3%, 28 patients), suggesting a potential influence of the PDA. However, drawing definitive conclusions is challenging since we lack data on patients' initial preferences before counseling or PDA use, making it difficult to ascertain the true impact of these interventions on treatment choices. Nonetheless, these findings underscore the potential of PDAs in healthcare decision-making, prompting further exploration and integration into clinical practice.

In comparison to the existing literature our PDA demonstrates a relatively favorable performance[37]. While a significant number of PDAs successfully improve patient knowledge, their effect on reducing decisional conflict is less consistent. This difference may be related to the complexity of medical decisions involved [38,39]. A systematic review investigating the effectiveness of PDAs in cancer-related decisions showed that most studies have similar results as we have found, indicating that PDAs are an improvement in cancer care[40]. This review did not include studies with head-and-neck cancer patients, making it difficult to compare studies. Specifically since head-and-neck cancer patients are frailer than patients with other solid malignancies[41].

Despite the study's promising outcomes, integrating PDAs into clinical practice poses notable challenges[37]. The gap between the potential benefits observed in research settings and actual deployment of PDAs in daily patient care highlights the complexities involved in adopting these tools on a routine basis. Factors such as logistical barriers, healthcare providers' attitudes, patient preferences, and institutional policies play a critical role in this challenge[42].

To bridge this gap, targeted efforts are necessary to overcome the hurdles to PDA implementation. This involves training healthcare providers in SDM and the effective use of PDAs, continues improvement and updating of the PDA, adapting clinical pathways to accommodate these tools, and fostering a culture that prioritizes patient involvement in decision-making[42,43]. Addressing these issues is crucial for ensuring that PDAs reach their full potential in supporting patients throughout their healthcare journey, making informed decisions a standard part of patient care.

This might lead to a situation in which treatment choices are based on personal preferences and informed decisions, which not only fosters a sense of autonomy but also reduces the risk of decisional regret and associated psychological distress, such as depression[44].

Limitations

Due to the low incidence of T3/T4 larynx cases in the Netherlands (approximately 300 cases per year[45]), we chose to concurrently start inclusion for the usual care arm during development of the PDA. However, this pre/post design can introduce bias compared to a randomized controlled trial (RCT). We tried to counter potential bias by using propensity score correction.

Patients in the intervention arm utilized the PDA at their own discretion and in their own setting. Unfortunately, data is not available on whether patients completed the entire PDA on their own, frequency of use, or if information was discussed with relatives. For patients (n=11) without internet access, the PDA was accessed on a hospital computer, potentially influencing their engagement, as they used the PDA just after the counseling consultation, potentially creating an overload of information.

This study did not explore whether patients altered their treatment preferences after utilizing the PDA, nor did it assess the effect of the PDA on patient involvement and decision regret. This limits our insights into the effectiveness of the PDA. Finally, SDM was only measured using self-report. We have no data on the frequency and quality of actual SDM behavior during consultations.

Conclusion

This multicenter prospective study examined the only PDA currently available for patients with advanced laryngeal cancer worldwide. The PDA enhanced patients' understanding of disease and treatment options, improved their perceived level of Shared Decision-Making, and reduced decisional conflict. These outcomes support the incorporation of this PDA into standard care protocols to empower advanced laryngeal cancer patients during their counseling period, marking a significant step towards more patient-centered healthcare.

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Chapter 6

The Development of a Decision Aid for Patients with Operable Oropharyngeal Carcinoma in the Netherlands – A Mixed Methods Study

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Abstract

Objective: The aim of this project is to create an interactive online patient decision aid (PDA) for oropharyngeal cancer (OPSCC) patients, eligible for transoral (robotic) surgery with an ultimate goal to assist both physicians and patients in making treatment choices.

Materials and methods: Following the International Patient Decision Aid Standards, a mixed-methods approach was employed. The study involved semi-structured in-depth interviews with patients and physicians, thinking-out-loud sessions, and study-specific questionnaires. Thematic coding and analysis were conducted on verbatim transcriptions of audio-recorded interviews.

Results: The PDA drafts were evaluated by twenty OPSCC survivors and twenty multidisciplinary specialists. Significant revisions were made after phase 1 to enhance readability and reduce text, whilst incorporating videos and graphics. Following all phases, both patients and specialists rated the PDA as comprehensible, feasible, and a valuable addition to regular counseling.

Conclusion: This study showcases the development of a PDA for early stage oropharyngeal cancer patients considering surgery and radiotherapy options. The decision aid emphasizes the disparities in short- and long-term side effects between the two treatments. Patients and physicians found the decision aid to be understandable, user-friendly, and helpful for future patients. The PDA is available on https://beslissamen.nl/**.**

Keywords: Shared decision-making; Counseling; Communication; Head and neck cancer; Oropharyngeal cancer; Human Papilloma Virus

Competing interests: None declared

Introduction

There has recently been a shift in the epidemiology of oropharyngeal squamous cell carcinoma (OPSCC) in the Western world. Formerly, tobacco and alcohol were the main risk factors, but prevention campaigns have reduced their prevalence[1, 2]. At the same time, human papillomavirus (HPV) has emerged as a new risk factor, causing a significant increase in the incidence of OPSCC[3, 4]. HPV-related tumors are now responsible for most (70%) OPSCCs in Europe[5]. HPV-positive early stage OPSCC patients, typically younger and healthier, are expected to have excellent long-term survival. Nowadays the most applied treatment modalities for early-stage OPSCC are either radiotherapy to the oropharynx and neck, or transoral (robotic) surgery (TO(R)S) including a neck dissection if indicated. Single modality treatment is preferred for early-stage OPSCC to minimize morbidity and costs[6].

To date, retrospective studies have found no significant difference in survival and oncologic outcomes among these treatments[3, 7]. Prospective data on long-term functional outcomes reveal similar quality of life (QoL) outcomes, but differences in toxicities[6, 8]. But even with these new insights, patient and clinicians face the difficulty and complexity of appropriate treatment selection to meet individual patient preferences. This emphasizes the importance of shared decision-making (SDM). Patient decision aids (PDAs) are interventions supporting patients in their decision-making process and have proven to be effective in making patients more knowledgeable, better informed, show insight in patient values and more accurate risk perception[9, 10]. There are several existing PDAs for different cancer types. In Head-and-Neck Oncology there is a PDA for advanced laryngeal carcinoma developed in our center[11], and a PDA for oropharyngeal cancer from the United States[12]. Since patients' values, preferences but also treatment guidelines are dependent on country and culture, we decided to develop our own PDA for patients with early stage OPSCC that are eligible for curative treatment with either transoral (robotic) surgery or radiation therapy.

This study describes the assessment of the preferences and needs of early stage OPSCC patients and their healthcare providers, facing a single modality treatment choice, in The Netherlands. A PDA was developed, and its usability and feasibility was tested to make the PDA usable in daily practice.

Materials and Methods

This is a multicenter study, based on the criteria for developing a PDA as set by the International Patient Decision Aids Standards (IPDAS) Collaboration[13, 14], following the three development phases (see Figure 1).

The scope of the PDA was determined by the research group, based on clinical experience and literature. The PDA was developed for patients with early stage OPSCC making a primary curative treatment choice between radiation therapy and transoral (robotic) surgery (TO(R)S) with or without neck dissection (ND). The purpose of the PDA was to give an overview of the disease, treatment possibilities and side effects, and improve understanding.

The multicenter multidisciplinary steering group consisted out of the following disciplines: Radiation Oncology, Speech-and-Language Pathology, Head-and-Neck Oncology and Surgery, Physiotherapy and Rehabilitation. The role of this group was to review preliminary results and content, and provide guidance through all phases of the development process.

Phase 1 consisted of multiple steps. Most recent trials investigating primary surgery and radiation in early stage OPSCC were reviewed and compared with counseling materials. Furthermore, semi-structured in-depth interviews with patients and physicians from six head-and-neck centers were held to evaluate patients' decisional needs and the regular counseling process. Inclusions were stopped after reaching data saturation. All collected data was used to construct the first version of the PDA by a web designer with experience in developing decision aids.

In phase 2, the comprehensibility and usability of the PDA was alpha tested. This was done through interviews with patients and physicians, and thinking-out-loud sessions whilst showing the PDA. Afterwards everyone filled in a study-specific questionnaire with 35 statements regarding evaluation of the PDAs usability, comprehensibility, content, added value, design and satisfaction. All statements were positively framed and ranged from totally disagree (1) to totally agree (5). The questionnaire was followed by three open questions for feedback regarding points that participants liked, disliked, and suggestions for improvement. Ending with a ranking of the PDA ranging from 0-10, where a score ≥5.5 was a passing grade.

Phase 3, entailed a similar routine as phase 2, more focusing on the improvements and therefore feasibility. This was tested with the same method and tools as in phase 2.

Due to the Covid-19 pandemic, phase 2 and 3 were performed through video calls and questionnaires were sent via email or post as preferred by participant.

Recruitment and inclusion criteria

Previously treated patients were recruited by their treating physician and subsequently contacted by the researcher (A.H.). Patients needed to have been eligible for primary radiation therapy or TO(R)S with or without a neck dissection. This was decided during the multidisciplinary team (MDT) meeting, taking into account the patient's clinical profile, tumor stage and location, imaging results, and pathological examination. A crucial aspect was to minimize the risk of adjuvant treatment after surgery. OPSCC-treating physicians were recruited through peer networking. All participants signed informed consent.

Scope of the PDA

The PDA was developed for patients facing a single modality treatment choice. The Dutch oral cavity and oropharyngeal carcinoma guideline was published in 2014 and is therefore outdated (update expected to be published in 2023-2024). Involved centers have made their own guidelines based on literature, local resources (e.g. availability of TORS) and experiences. It was therefore decided not to limit inclusion criteria by tumor stage, but to follow the decision of the local MDTs whether a patient was suitable for unimodality treatment (radiation or TO(R)S). The PDA is meant for patients with stage I HPV+ OPSCC and stage I-III HPV- OPSCC where primary tumors are resectable transorally and neck disease is very limited.

Data processing and statistics

All interviews (in depth, and thinking out-loud sessions) were performed by A.H., who had no treatment relationship with the patients. The interviews were audio-recorded, verbatim transcribed, and anonymized. Thematic coding was done using ATLAS.ti software (version 9.1). Thematic coding leads to the discovery of appropriate content for the decision aid focusing on the decision-making process, experiences around side effects of treatments, knowledge about the disease, (decisional) needs and opinions about the PDA. The results of the questionnaire were quantitative data and are displayed using means, ranges, and percentages.

Ethics

This study does not fall under the scope of the Medical Research Involving Human Subjects Act and was approved by the review board of the Netherlands Cancer Institute (IRBd18-030).

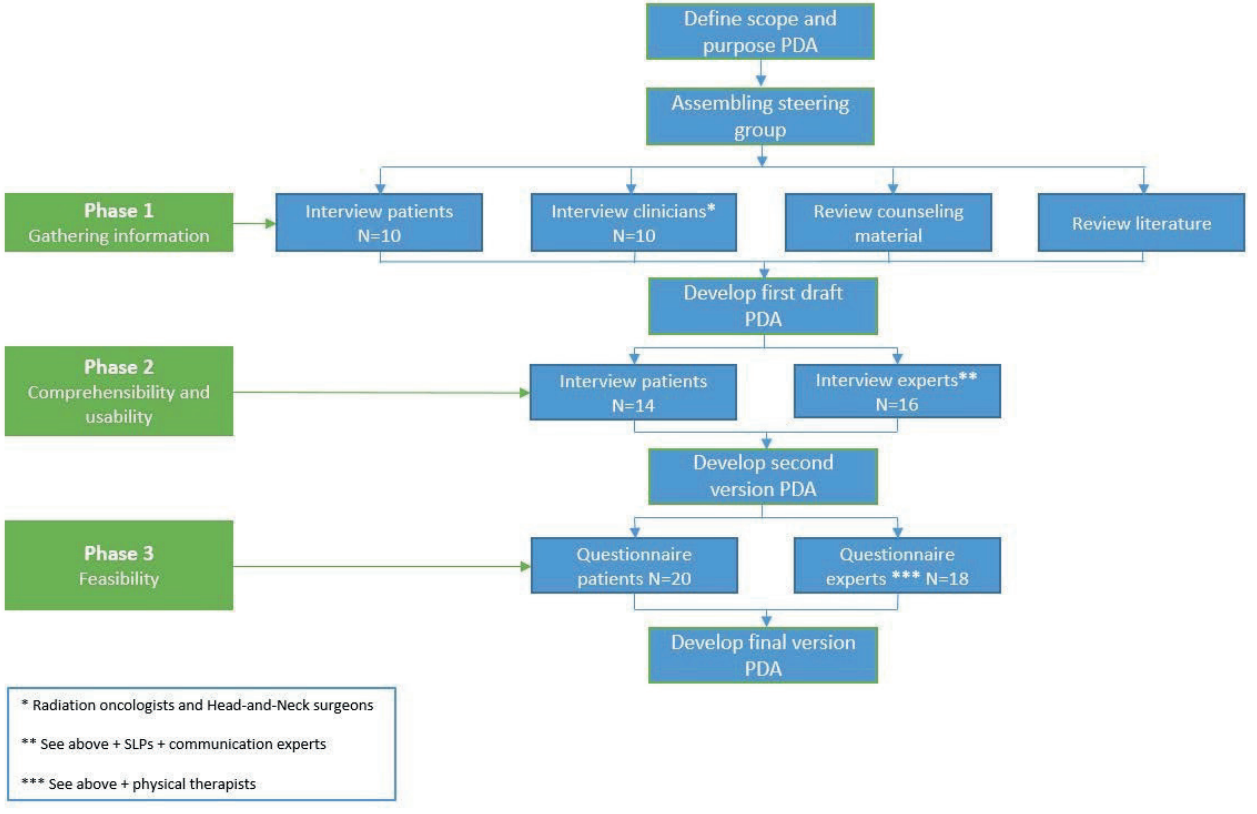

Figure 1. Developmental phases

Flowchart of all developmental phases following the IPDAS criteria. SLP = Speech-Language-Pathologist, IPDAS = International Patient Decision Aid Standard, PDA = Patient Decision Aid.

Results

Characteristics

All characteristics can be found in table 1. Of all selected patients, two refused participation. All healthcare providers came from six different Dutch Head-and-Neck Centers and the medical Communication Experts (CE) from two Dutch universities.

Table 1. Participant characteristics

	Patients
Age	
(mean, range)	60 years (46 - 81)
Gender	
Female	7 (35%)
Male	13 (65%)
Education level	
Primary	4 (20%)
Lower secondary	7 (35%)
Higher secondary	5 (25%)
University*	4 (20%)
Tumor stage	
I	13 (65%)
II	4 (20%
III	3 (15%)
HPV	
Positive	12 (60%)
Negative	8 (40%
Treatment	
RT	12 (60%)
TOS	1 (5%)
TORS + ND	5 (25%)
TO(R)S + PORT	2 (10%)
Years since diagnosis	
(mean, range)	4 years (1 – 11)
Included per phase	**N (%), N cumulative**
Phase 1	10 (50%), 10
Phase 2	4 (20%), 14
Phase 3	6 (30%), 20

Table 1. Continued

	Experts
Age	
(mean, range)	46 years (30 – 59)
Gender	
Female	10 (50%)
Male	10 (50%)
Specialty	
RO	7 (35%)
HNS	7 (35%)
SLP	2 (10%)
PT	2 (10%)
CE	2 (10%)
Work experience	
(mean, range)	14 years, (5 – 26)
PDA experience	
None	4 (20%)
One	14 (70%)
Multiple	2 (10%)
Included per phase**	**N (%), N cumulative**
Phase 1	10 (50%), 10
Phase 2	7 (35%), 16
Phase 3	3 (15%), 18

*Of which 1 patient obtained a doctorate. ** The numbers do not add up to 20 because one RO only participated in phase 1 and one SLP only participated in phase 2. ND = neck dissection, RT = radiation therapy, TO(R)S = transoral (robotic) surgery, PORT = post-operative radiation therapy, RO = radiation-oncologist, HNS = Head-and-Neck surgeon, SLP = speech-and-language pathologist, PT = physiotherapist, CE = communication expert

Phase 1: Gathering information

Literature and Counseling materials

We focused on randomized studies comparing radiation and surgery in early-stage OPSCC. The 'ORATOR trial'[15] and the 'BEST OF' trial[16] are both studies investigating the best treatment for this patient group. The 'BEST OF' trial is still ongoing. Results of the 'ORATOR' trial are analyzed and compared to our 'inclusion criteria' and used as background information. Preferably we wanted to use Dutch survival rates, but there were no reliable numbers available. After discussion with the steering group, it was decided that the survival numbers from the 'ICON-S' study are most accurate and therefore used in the PDA[17].

None of the interviewed Head-and-Neck Surgeons (HNS) used counseling materials during their consultations. Some of them use patients' scans or drawings to clarify where the tumor is situated, and explain treatments. Radiation Oncologists (RO) did have flyers and brochures about radiation in the HN area, however, used them rarely.

Physicians
Five HNS and five RO were included from four Dutch Head-and-Neck centers. Interviews lasted on average 26 minutes (range 22 – 35). All agreed that a PDA would be a valuable addition for the decision-making process in this group, and that the main goal should be to avoid multimodality treatment to minimize treatment morbidity. There were different opinions regarding the occurrence of side effects and their severity.

Patients
Ten patients were interviewed, which lasted on average 36.21 minutes (range 21.58-50.08). All patients initially stated that survival is the most important in decision-making, but after hearing survival is similar regardless of treatment modality, side-effects were mentioned as the leading factor in choosing treatment.

Prototype development PDA
The results of the selected literature, counseling materials and interviews were used to develop the first draft of the PDA. See figure 2.

Phase 2: Alpha testing of the Comprehensibility and usability
Experts
Sixteen experts evaluated the first draft, each focused mainly on their specialty (see table 3). There was a discussion about HPV-status, and it was decided to make three versions of the PDA (HPV positive, negative, unknown) in which there would be different information regarding the etiology, risk factors, and survival. For HPV status 'unknown', survival numbers for HPV positive and negative are displayed. On a scale of 1 to 10 (worst to best, where ≥5.5 is sufficient) this draft of the PDA was rated 7.1 (median, range 6.0-7.5).

Patients
Fourteen patients went through the PDA during a thinking-out-loud session and completed a questionnaire. The PDA was rated as an easy-to-navigate website. They rated this draft a 7.9 (median, range 7.5-9.5).

Table 2. Themes observed in interviews

Themes	Patients	Physicians
General results interview	1) Fear of death 2) Overwhelmed by information 3) Want to start treatment as soon as possible	1) Difficult to relay important information without giving too much information 2) Make clear that survival is relatively good 3) State treatment possibilities
Survival	1) Most important, but since it is quite similar for both treatments it is not decisive in decision-making	1) As far as we now know from research, both treatments give similar oncological outcomes
Side-effects	1) Initially mostly focused on short-term side effects 2) After learning long-term side-effects they are viewed as most important for decision-making 3) Most feared is persistent swallowing problems 4) Most patients in hindsight missed information about dental problems, hair loss and risk of radiation after surgery	1) Multimodality treatment gives more and more severe side effects, so unimodality treatment is preferred 2) Differences in the long term should be explained to patients for decision-making 3) Specialists mainly explain side-effects of their own treatment modality
Side-effects management	1) Most focused on short-term side effects such as pain (painkillers) 2) Not familiar with the support options provided by paramedics and that this is also possible after completion of treatment	1) Important to explain side effects and their management such as treatment by SLPs and dieticians

SLP= Speech-Language-Pathologists

Phase 3: Beta testing of the Feasibility

Experts

Eighteen experts evaluated the last version of the PDA. Negative aspects were that the total duration to go through the PDA was rated as quite long (mean 21 minutes, range 12-45). Positive were the layout, structure of the website, and the addition of videos and graphs. All experts (n=18) found the PDA feasible and a valuable addition to regular counseling. They rated this version of the PDA a 7.9 (median, range 7.5-8.5).

Figure 2. First prototype of the PDA (in Dutch)

Information about risk factors for developing OPSCC. It shows the additional information which appears when one clicks on the question mark in the right corner

Patients

Twenty patients evaluated the final draft of the PDA. Patients reported that the time required to complete the final draft was appropriate (mean 37 minutes, range 15-60). All patients (n=20) were satisfied with the feasibility and wished they had seen this PDA during counseling. They graded this version of the PDA with an 8.7 (median, range 8.0-10.0).

Final version of the PDA

The final version consists of several components, including a narrated slideshow that gives an overview of early stage OPSCC and its treatments along with their corresponding side effects. Additionally, there were side-by-side comparisons of the treatments, videos featuring physicians explaining treatments, side effects and their management, as well as videos of survivors detailing their personal experiences. The PDA also contained knowledge-based and personal value-based questions, as well as a printable worksheet where patients could record their answers and add additional questions to discuss with their physician. An appendix containing definitions of important terms was included, along with a page that provided patients with additional information, if needed.

The final version of the tool is available on https://beslissamen.nl/. This is a Dutch website that hosts multiple PDAs.

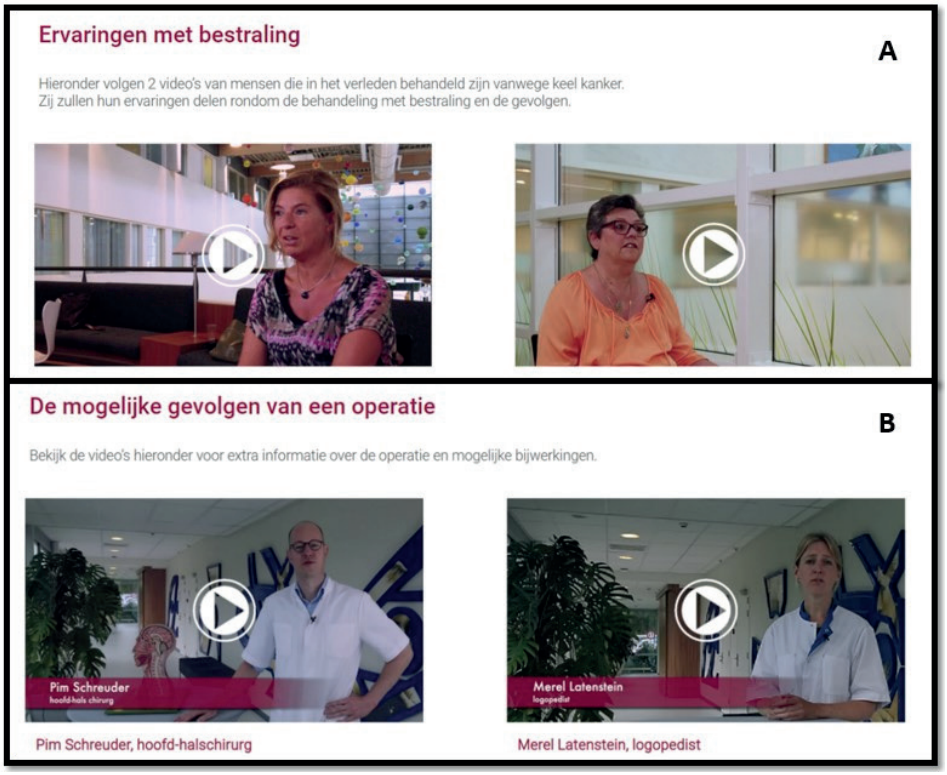

Figure 3. Overview of used videos instead of text.

A: Videos of the experiences of patients with radiation. There are also videos of patients surgically treated. B: Videos in which the consequences of the surgery are explained by a head-and-neck surgeon and a SLP. These videos are also available about radiation therapy and are explained by a radiation-oncologist and a SLP.

Table 3. Overview of the development of the PDA per phase, and quotes

	Patients	Physicians
Phase 1	• Survival is the most important outcome • Side-effects should be the leading factor in choosing type of treatment • Receiving the diagnosis is overwhelming and stressful • Most received information was too extensive and complex • 70% of the patients did not feel well informed after counseling • 50% of the patients was not aware surgery could be a potential treatment	• All agreed that a PDA would be a valuable addition for the decision-making process • The main goal should be to avoid multimodality treatment to reduce treatment side effects
Phase 2	• 12/14 (86%) stated there was too much text, which hampered focus and the use of the PDA • 8/14 (57%) mentioned that the used level of language was too complex • All patients stated that more graphs and videos would make the decision aid easier and more accessible for everyone	CE: language level was too complex to be accessible to all. Also, the amount of text was too much, and the use of graphs and videos was too limited SLP: the amount of information was rated good, but more focus is needed on the management of potential side effects PT: information on nerve palsy after neck dissection is lacking HNS en RO: both wished to add more information regarding side effects and risks related to the treatment of the other specialty Overall: The decision aid should be adjusted for HPV status (positive, negative, and unknown)

Quotes	Adjustments
• HNS 2 (F, 51y): *"It is complex and difficult to determine which treatment is best for this group, also for us as physicians. You want to give the treatment that does the least harm, but up until now it remains unclear which treatment has least side-effects. Therefore, it is important to know patients' preferences and to inform them about both options, so that the patient, together with family or friends, and of course with our guidance, can make a choice in the treatment that suits him or her best."* • RO 7 (F, 50y): *"My ultimate goal is to ensure that patients do not have to undergo multimodality treatment and therefore experience as few side effects as possible. With surgery, there is a potential risk for the need of adjuvant radiotherapy either to the neck or the primary site in case of inadequate margins or involvement of multiple lymph nodes or extra capsular spread. It is important that the patient is aware of this as part of treatment decision making."* • Patient 7 (F, 62 years): *"When I received the diagnosis and information about treatments, I could not remember a thing that was said. All the appointments were on the same day, and everyone was using such difficult language. It was also because of the stress, but it was also just too much for me, and therefore I did not feel prepared for the treatment."*	• The results of the literature search, counseling materials and interviews were used to develop the first draft of the PDA. • Simultaneously the first prototypes were designed.
• CE 1 (F, 54y): *"Unfortunately, medical terminology is still widely used during counseling. This is often complicated information and can create patient anxiety and therefore make them reluctant to ask questions. It is so important that treatments are explained in understandable language, and preferably visually assisted to improve intelligibility for every patient."*	• Rewriting and concision of text (language level B1)[18] • Replacing text with graphics, animations and videos • Recording of videos in which survivors tell about their experiences • Information on nerve damage during a neck dissection was added

Table 3. Continued

	Patients	Physicians
Phase 3	• The amount of time needed to finalize the final draft was in the right proportion (mean 37 minutes, range 15-60) • Patients who received RT as treatment stated they would like more information to be added on the potential side effects on dental status and loss of hair in the radiated area • All patients (n=20) were satisfied with the feasibility and wished they had seen this PDA during counseling	• The videos are too long, and the possibility to be paused and exit the videos should be added • The total duration to go through the PDA was rated as quite long (mean 21 minutes, range 12-45)

PDA = Patient Decision Aid, RO = radiation-oncologist, HNS = Head-and-Neck surgeon, SLP = speech-and-language pathologist, PT = physiotherapist, CE = communication expert

Quotes	Adjustments
• HNS 8 (M, 61y): *"The goal of the decision aid should be to enable the patient to weigh and consider various aspects of the treatment. During my consultations I always discuss surgery and the associated quality of life. Is that acceptable for them, even if it is unsure? Then we will operate. Interestingly, patients often express that they prioritize quality of life. But controversially they can state they prioritize survival. Hopefully, by providing patients with a clearer understanding through the decision aid, they can make more informed choices".* • SLP. 2 (F, 36y): *"Important is that patients know that we are here to support them in the side-effects that they will endure during and after treatment, but also what kind of side-effects they can expect."*	• Videos are shortened and can be paused and stopped • Added the possibility to skip parts in the PDA (only for the general information about the disease) • Added information about teeth extraction, hair loss in radiation field • All text was recorded to create the opportunity to listen to the information and make the PDA more accessible

Discussion

This study outlines the development and feasibility testing of the first Dutch multidisciplinary PDA for patients with an early stage OPSCC) who are eligible for both treatment with radiation therapy or transoral (robotic) surgery with or without ND, as a single modality treatment with curative intent. Experts and patients perspectives were carefully considered during the development of this tool, which underwent extensive editing to ensure it was easy to understand, usable, feasible, and well-designed. With the incidence of OPSCC on the rise and a lack of consensus regarding radiation- versus surgery-based treatments, our PDA offers a helpful framework for newly diagnosed patients to make treatment decisions that align with their personal values but also increase their knowledge on the disease, treatment and possibilities.

Increasing attention is being given worldwide to the implementation of shared decision-making and associated tools; in the Netherlands this is an important topic in the vision document "Medical Specialist 2025" of the "Federation of Medical Specialists"[19]. Additionally, a campaign called "Start a Good Conversation" was launched in 2022, focusing on shared decision-making. This collaborative effort involves various organizations including the Federation of Medical Specialists, General Practitioners Association, Ministry of Public Health, Welfare and Sport, Dutch Association of Hospitals, Patients Federation, and Health Insurers[20]. The campaign offers guidance for healthcare providers and patients to facilitate shared decision-making, as well as opportunities for collaborative development of decision aids and other tools.

In the Netherlands, multiple PDAs for several medical purposes have been developed, but for head-and-neck oncology only a PDA for advanced laryngeal carcinoma is available, of which the impact is still being studied[11]. One could state that decision aid tool development for head and neck cancer is falling behind compared to other oncological diseases[21-25].

We found that all patients were aware of radiation treatment, but not all were aware of the option of surgical treatment. This is quite interesting considering they were eligible for both, as judged by the multidisciplinary tumor board. It is unclear if both treatments were not discussed, or if patients have forgotten this information, referred to as 'recall bias'[26]. Important factors for decision-making for patients were clarity regarding equal survival numbers for these two treatments, focus on differences in short-term side-effects, but most important long-term side-effects. A research group from the Johns Hopkins hospital developed a PDA for OPSCC patients and also found that patients primarily focus on survival. Most of their patients felt well informed by

their physicians, whereas our patients felt overwhelmed and the used language was too technical and therefore too difficult[12, 27]. Another PDA for OPSCC has been developed in Ontario[28]. They developed the PDA with healthy volunteers and focused on their treatment preference, showing a preference for TORS above radiation, based on the side-effects.

Our study reveals that both patients and physicians perceive the PDA as a valuable supplement to traditional counseling. However, notable distinctions arise between physicians and patients. Physicians tend to prefer offering extensive information, whilst patients express concerns about information overload. On the other hand, physicians report perceiving the time required to utilize the decision aid as relatively high, whereas patients rate it favorably. Once again, this underscores the importance of collaborative efforts between physicians and patients, particularly considering the substantial evidence indicating that patients and physicians prioritize different aspects of disease and treatment[29-31]. Physicians were satisfied with the results and most of all with the use of videos and graphics. For successful utilization, an effective implementation plan is crucial, particularly in determining how the PDA will be used: whether during counseling sessions with doctors, in collaboration with specialized nurses, or even in the comfort of one's home.

Evaluation of patients' preferences is a difficult task and is quite often overlooked or forborne in the era of national guidelines and results from multidisciplinary meetings in which strong emphasis is placed on survival outcomes. Furthermore, treatment choices can be highly dependent on the type of information provided during counseling. As physicians have limited consultation time, and physicians find it difficult to assess patients' treatment preferences, levels of shared decision-making are low[32, 33]. This might result in decision regret since patients are not aware of treatments and might undergo a treatment that is not fitting their preferences[34, 35]. Tools like this PDA will be a perfect solution to bridge this gap.

Limitations

As a result of the COVID-19 pandemic, our study was limited to including patients solely from The Netherlands Cancer Institute. Additionally, the second and third phases had to be conducted remotely via phone or digital means, although the ideal scenario would have been in-person interactions. Literature comparing TORS and radiotherapy in this type of OPSCCs was scarce during the first phase of this study. A more recent study (which was not available during the development of this PDA) about long-term results of the ORATOR trial showed that swallowing difference between primary radiotherapy and TORS approaches persists but decreases over time[8]. It is worth

noting that the educational level of the participating patients surpasses the average level in the Netherlands. Nevertheless, with the assistance of the patient society and communication experts, we ensured the accessibility of the PDA for individuals from diverse backgrounds, but at this moment only in Dutch. However, further testing on new patients presenting with early oropharyngeal cancer is yet to be conducted.

Conclusion

We developed a Dutch multidisciplinary patient decision aid focusing on treatment decisions for oropharyngeal tumors for whom primary transoral (robotic) surgery could be a curative treatment, following the quality criteria of IPDAS[36]. This web-based tool has shown to be feasible and an addition for regular counseling, as assessed by clinicians and OPSCC survivors.

To this end, a multicenter trial has started in 2022 comparing regular care to patients receiving the PDA (www.kanker.nl, trial 1339) to investigate the effect of using a PDA in daily practice on patient knowledge and decisional conflict. Results are expected in 2026.

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Part 2
Rehabilitation after
Total Laryngectomy

Chapter 7

Does Prophylactic Replacement of Voice Prosthesis Make Sense? – A Study to Predict Prosthesis Lifetime

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Abstract

Objective: Voice prosthesis leakage significantly impacts laryngectomized patients' quality of life, causing insecurity and frequent unplanned hospital visits and costs. In this study, the concept of prophylactic voice prosthesis replacement was explored to prevent leakages.

Study Design: Retrospective cohort study

Setting: Tertiary hospital

Methods: Device lifetimes and voice prosthesis replacements of a retrospective cohort, including all patients laryngectomized between 2000 and 2012 in the Netherlands Cancer Institute, were used to calculate the number of needed voice prostheses per patient per year when preventing 70% of the leakages by prophylactic replacement. Various strategies for the timing of prophylactic replacement were considered: Adaptive strategies based on the individual patient's history of replacement and fixed strategies based on the results of patients with similar voice prosthesis or treatment characteristics.

Results: Patients used a median of 3.4 voice prostheses per year (range 0.1-48.1). We found a high inter- and intrapatient variability in device lifetime. When applying prophylactic replacement, this would become a median of 9.4 voice prostheses per year, which means replacement every 38 days, implying more than six additional voice prostheses per patient per year. The individual adaptive model showed that preventing 70% of the leakages was impossible for most patients, and only a median of 25% can be prevented. Monte-Carlo simulations showed that prophylactic replacement is not feasible due to the high Coefficient of Variation (Standard Deviation/Mean) in device lifetime.

Conclusion: Based on our simulations, prophylactic replacement of voice prostheses is not feasible due to high inter-and intrapatient variation in device lifetime.

Keywords
Voice prosthesis, voice rehabilitation, total laryngectomy, prosthetic leakage, device lifetime

Introduction

In most Western countries, the most successful technique for voice restoration after Total Laryngectomy (TL) is tracheoesophageal (TE) prosthetic speech[1]. The most commonly used voice prostheses (VPs) are indwelling VPs, which can be categorized as regular and problem-solving VPs. Regular VPs are the most commonly used for laryngectomized patients. In case of frequent short device lifetimes the so called problem-solving VPs are indicated. Regular VPs are expected to have a median lifetime ranging from 2 to 6 months[2,3]. Soolsma et al. showed that problem-solving VPs have a 16-fold longer device lifetime than regular VPs (median device lifetime 337 days)[4].

The main reason for VP replacements is transprosthetic leakage (55-80%), followed by periprosthetic leakage (5-30%) [5–8]. The frequent replacements significantly impact the patient quality of life, causing insecurity and unplanned hospital visits and costs. [9]. The standard policy for replacements is Wait-to-Leakage (WtL), but possibly the replacements can be planned to prevent leakage (prophylactic replacement). The principle of prophylactic replacement has been used in pacemaker users for years. This has given pacemaker users the security of a continuously working device [10,11]. The device lifetime of pacemakers depends on the battery. The device lifetime of VPs depends on many more aspects such as the ability of a patient to clean the VP properly, type of VP, biofilm formation, shrinking TEP, hypertrophy, infection, etc. But also distance to the hospital, voice problems, diet, having a partner, country of origin have been found to be related to device lifetime[3,12–18].

The aim of the present study was to explore the possibility of prophylactic voice prosthesis replacement (PVPR) by predicting VP lifetime and calculating the needed number of VPs when applying PVPR using these predictions.

Materials and Methods

In this study, a retrospective database was used [3]. All included patients (n = 242) were laryngectomized between January 2000 and December 2012 and in regular follow-up in the Netherlands Cancer Institute. The last date of follow-up was January 05, 2017.

After the initial inclusion of 242 patients, patients with less than two VPs replacements or no follow-up data were excluded. This resulted in 194 included patients (figure 1). Patients were analyzed based on the used type of VP and indication for TL. All VPs analyzed in this article are manufactured by Atos Medical AB (Hörby, Sweden). Analysis were done for the total group and two subgroups. The following data were collected for each VP replacement: date of insertion, replacement or removal, type and size of the VP, and the reason for replacement or removal. VPG1 beholds patients only using regular VPs (Provox2 or Provox Vega). VPG2 are patients alternating between regular and problem-solving VPs (ActiValve Light, Strong or Xtra Strong). There were no patients only using problem-solving VPs.

Patient Group 1 (PG1) underwent primary laryngectomy with or without additional treatment. Patient Group 2 (PG2) had either a salvage laryngectomy for recurrence, second primary tumor or a laryngectomy for a functional reason. All VP replacements were performed by qualified and trained speech-language-pathologists, residents or Head-and-Neck surgeons.

Statistical analysis

Descriptive analysis was used to summarize patient and device characteristics. The VP lifetime was measured in days, calculated from the insertion date to the date of removal or last follow-up date. Kaplan Meier analyses were used to assess device lifetimes and a moment for prophylactic replacement. Device lifetime of VPs ongoing at the end of the observation period are right-censored, as well as device lifetimes of VPs still in situ when the patient was lost to follow-up or died. Standard deviations (SDs) were used to describe variability in device lifetime, and Mann-Whitney-U was used to test for differences in device lifetime and variability. Statistical analyses were performed in R version 4.1.0 and SPSS version 27.0.

Prophylactic voice prosthesis replacement prediction model

In this study PVPR is considered feasible if at least 70% of VPs are replaced before leaking, allowing a 30% leakage fraction as acceptable. This cut-off point is chosen by consensus of the research team and called DeviceLife70 (DL70, expressed in days). The current standard policy (Wait to Leak, WtL) has a 100% leakage fraction. To train the prediction

model, the DL70 was chosen as the number of days at which the Kaplan-Meier curve for device lifetime in the different type of groups of patients crosses the 70% boundary. Several models were considered: one DL70 for all patients, separate DL70s for used type of VPs (VPG1 and VPG2), and separate DL70s for indication TL (PG1 and PG2). All models assume that problem solving VPs will never be prophylactically replaced.

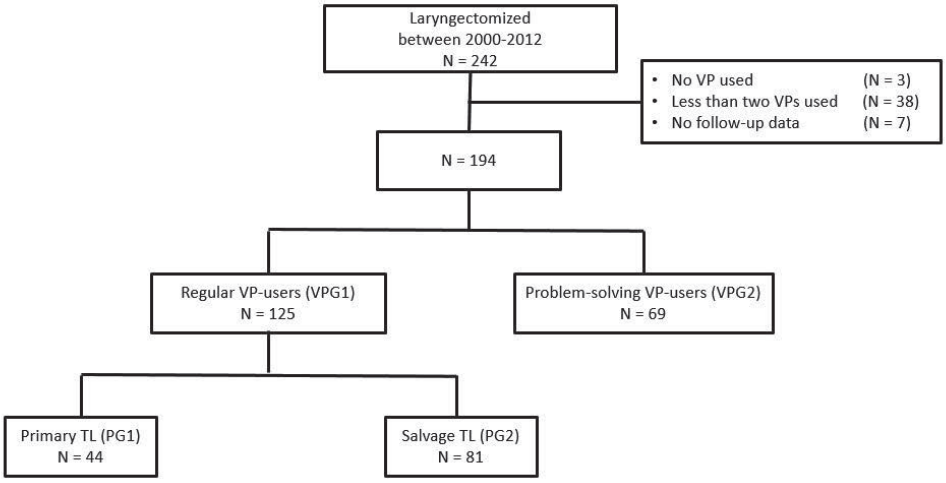

Figure 1. Flowchart of included patients and subgroups

Abbreviations: VP=voice prosthesis, TL=total laryngectomy

For evaluation of the prediction models, we counted how many of the VPs received by the patients would be prophylactically replaced and how many would (still) have been replaced because of leakage if the various prediction models had been used at the time. VPs with a device lifetime shorter than DL70 are considered 'replaced because of leakage.' VPs with a device lifetime at DL70 or higher are considered 'prophylactically replaced.' Time in situ of additional VPs (that would be used in case of PVPR) was estimated from known history of VP use per year. Thus, for each patient the number of needed VPs per year under the various prediction models were calculated. In the evaluation of the model that uses different DL70s for VPG1 and VPG2 we assume that all patients start in VPG1 and switch to VPG2 as soon as they have their first problem solving VP. The data is displayed in medians and ranges.

Individual adaptive simulations

As there is a high device lifetime variability, an individual adaptive model per patient was made. This model uses the device lifetime of the first three used VPs to calculate the replacement moment for the coming VP, as the DL70 based on these three VPs.

After each replacement because of leakage, the moment of replacement for the next VP will be calculated as the DL70 on the then last three VPs. When the current VP reaches this moment and hence would be replaced prophylactically, the next moment of replacement will be the DL70 based on the last three VPs increased with 17% to correct for the fact that the actual lifetime of the last VP is longer than its in situ time. The value of 17% of this correction factor has been found by trial and error. Problem-solving VPs are not prophylactically replaced because of their longevity.

Monte-Carlo simulations

Since VP replacement data is sparse, the possibilities for leakage reduction by simulating device lifetimes through Monte-Carlo (MC) simulations was investigated. The main unknown factor in formulating an optimal device change policy is the probability distribution of the in-vivo device lifetimes. These MC-simulations are used to investigate the relationship between variability in device lifetime (inter- and intrapatients) and the limits of PVPR. The relevant parameter of this unknown probability distribution is the Coefficient of Variation (CV = Standard Deviation/Mean). The MC simulations model the average time between leakage events, relative to the default policy and the associated number of device replacements as a function of the simulated CV. The simulations are repeated for four probability distributions. See supplemental information for details.

Ethical considerations

This study does not fall under the scope of the Medical Research Involving Human Subjects Act and was approved by the review board of the Netherlands Cancer Institute (IRBd21-092).

Results

Patient characteristics

The patient, tumor, and treatment characteristics of the 194 patients are shown in table 1. The majority of the patients were male (79%), and the mean age was 63 years (SD 10.8). Most patients had laryngeal carcinoma (72%), and the majority were treated with (chemo)radiotherapy (67%) before TL. Half of the patients underwent a bilateral neck dissection during TL.

The median overall survival (OS) was 60.8 months (95% CI 38.7 – 82.9). The mean follow-up time was 66.4 months (95% CI 58.5 – 74.3).

Table 1. Patient, tumor, and treatment details of all patients (n = 194)

	No. of patients (%)
Sex	
Male	153 (79%)
Female	41 (21%)
Mean age (years)	62.8 (SD 10.8)
Tumor-stage	
I	3 (2%)
II	18 (9%)
III	96 (50%)
IV	77 (39%)
Primary tumor site	
Larynx	140 (72%)
Hypopharynx	26 (13%)
Oropharynx	17 (9%)
Miscellaneous	11 (6%)
Indication TL	
Primary TL	7 (3%)
Primary TL + additional treatment(s)	56 (29%)
Salvage TL*	108 (56%)
TL for second primary	23 (12%)

Table 1. Continued

	No. of patients (%)
Pharyngectomy	
No (standard laryngectomy)	137 (71%)
Near-total	37 (19%)
Circumferential	17 (9%)
Unknown	3 (2%)
Neck dissection during TL	
No	49 (25%)
Unilateral during TL	48 (25%)
Bilateral during TL	95 (49%)
Unknown	2 (1%)
Reconstruction	
No (primary closure)	124 (64%)
Yes**	67 (34%)
Unknown	3 (2%)

Abbreviations: TL= total laryngectomy, *18 of these patients underwent salvage TL for a dysfunctional larynx, ** Varying reconstruction methods were used: Pectoralis major muscle (n=49), Free radial forearm flap (n=8), Gastric pull-up (n=7), Antero-lateral thigh flap (n=2), Latissimus dorsi flap (n=1).

Voice prostheses

The 194 patients used 3265 VPs in total during this study period. VPs with in situ times of less than one day (n=92), VPs of an unknown type (n=25), and VPs replaced for developmental study purposes VPs (n = 86) were excluded, leaving 3062 VPs for analysis.

Device lifetime

The median device lifetime of all VPs (N=3062) was 69 days. The median number of used VPs per patient per year was 3.4 (range 0.2 – 48.1).

Of the 194 patients, 125 used only regular VPs (VPG1), and 69 used both regular and problem-solving VPs (VPG2). The median device lifetime of regular VPs in VPG1 67 days, and in VPG2 is 57 days. This difference was found to be significant (Mann-Whitney-U, $p<0.05$). The longevity of problem-solving VPs is two-and-half times longer than regular VPs, namely 168 days.

VPG1 (regular VP-users) was subdivided into two groups. PG1: primary laryngectomy with or without additional treatments and PG2: salvage laryngectomy for recurrence, second primary tumor or a laryngectomy for a functional reason (see figure 1). The median device lifetime in PG1 was 81 days and in PG2 65 days. The Mann-Whitney-U test showed a significant difference in device lifetime ($P<0.01$).

Device lifetime cut-off points

For all groups the 70% cut-off point (DL70) was calculated, which was used for the calculations in the prophylactic replacement model and are shown in table 2.

Table 2. DL70 cut-off points for the PVPR model.

Patient groups	DL70
All patients	40 days
VPG1	41 days
VPG2	90 days
PG1	45 days
PG2	39 days

Variability in device lifetime

Device lifetimes showed great variability, both within and between patients. The median within patient SD of device lifetime in all patients was 64.5 days (range 1.4 - 909.3). For VPG1, the median within patient SD was 85.3 days (range 11.2 - 909.3), whereas, for VPG2, the median within patient SD was 53.6 days (range 1.4-667.4). This difference in SD of the device lifetime was significant (Mann-Whitney U, $p<0.05$). Note that all three cases the median within patient SDs are of the same order of magnitude as the (overall) median device lifetime, indicating a high Coefficient of Variation (see figure 2).

Prophylactic Voice Prosthesis Replacement

When applying PVPR to all patients, using the DL70 of 40 days, the calculated median number of used VPs per year was 9.7 VPs (range 9.1 - 48.1), implying more than six (6.2) additional VPs per patient per year (range 0.0 - 9.0) to prevent 70% of the leakage events. PVPR after 40 days in case of no leakage would lead to a net mean in situ time of 38 days in the set of all patients.

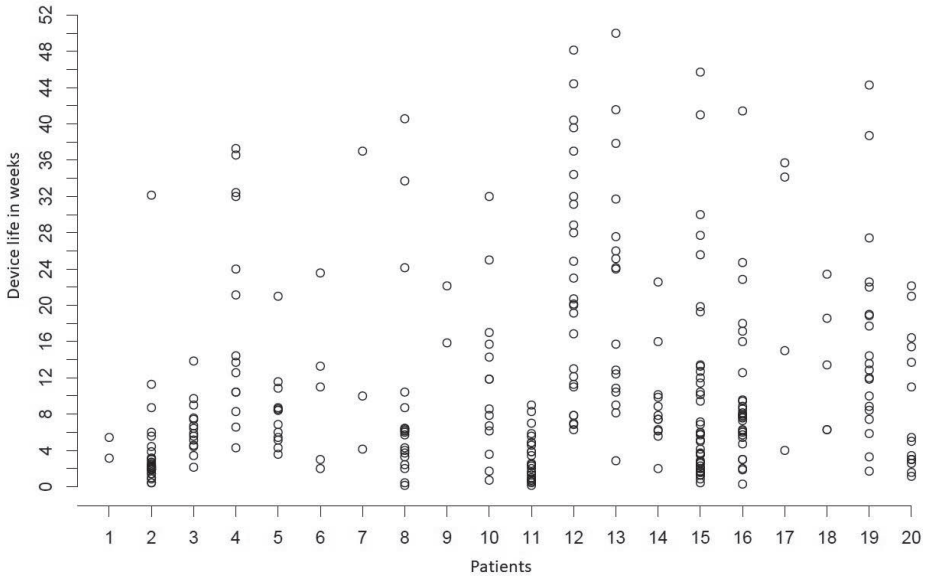

Figure 2. Overview of inter- and intrapatient variability of device lifetime of regular VPs in weeks. This is a representative sample of twenty regular VP-users (VPG1)

For regular VP–users (VPG1) the PVPR showed that patients would need 6 additional VPs replacements per year. The median used 3.4 VPs (range 0.1-48.1), and when applying PVPR 9.4 (range 8.9-48.1).For the indication TL subgroups, in PVPR, the median number of VPs was 8.6 (range 8.1-48.1) for PG1 and 9.7 (range 9.4-21.9) for PG2, but the additional number of VPs per year was 6.1 in both subgroups.

PVPR in an individual adaptive model

As described under methods the timing of prophylactic replacement is chosen to prevent 70% of leakages under assumption that the lifetime of the next VP is similar to that of the previous three VPs in the same patients. In our data we found a high intra-patient variability. We calculated the Coefficient of Variation (CV = SD/mean) and found a median of 0.8 (range 0.02 – 3.01). Due to this high intra-patient variability and the fact that the first three VPs will not be prophylactically replaced, in practice the prevention of 70% of leakage events is not reached in most study patients. Only nine out of 194 patients (4.6%) reached 70% prevented leakages. The median percentage leakage prevented by this method is 36% (range 0 – 81%). In the subgroup VPG1 of patients with only regular VPs the numbers are even worse: Median 25% of leakages prevented (range 81% - 100%).The patients in whom 70% of the leakage events could be prevented were patients with a high number of used VPs (range 21 – 57) during the study period.

PVPR in Monte-Carlo simulations

Monte-Carlo simulations were run for the DL70 case varying the Coefficient of Variation (CV = SD/Mean) between zero and one (See Supplemental Information). The results showed that for a CV > 0.5 the benefits in terms of decreased number of leakage events per year (<50%) decreased considerably while the costs in terms of additional VPs increased significantly (>163%). For a median CV of 0.8 as found in our patient base, there are around 20% less leakages per year requiring some 170% more devices. In this simulation, increasing the DL70 to a higher value can marginally decrease the number of leakage events but with a mounting increase in the number of devices needed.

Discussion

With this study we found that prophylactic replacement of VPs (PVPR) in laryngectomized patients is not feasible. PVPR would optimally reduce unexpected VP leakages and consequent aspiration and improve the quality of life of patients. To prevent at least 70% of all leakages in regular VP users, on average an additional number of six VPs per patient per year are needed, which is not desirable, given the costs and additional hospital visits.

Device lifetime differed significantly between primary TL (PG1) and salvage TL (PG2) but the number of additional VPs in PVPR was similar. The device lifetime of regular VPs in patients only using regular VPs (VPG1) is significantly longer than in patients alternating between regular and problem-solving VPs (VPG2), which is explained by the indication for problem-solving VPs (a short device lifetime with regular VPs)[3].

The high inter-and intrapatient variability in device lifetime (figure 2) makes it impossible to apply the concept of PVPR in daily practice. The device lifetimes are widely spread, and there is no clear trend visible, which is supported by the high standard deviation in device lifetime (median 64.5 days), which is around the median device lifetime, causing the high Coefficient of Variation (CV= SD/mean, median 0.8). The individual adaptive simulations showed that only 25%-36% of the leakages can be prevented. The Monte-Carlo simulations showed that PVPR would only be valuable if the CV is < 0.5, again stating that PVPR is not possible in real life.

As mentioned, prophylactic replacement has been successful for pacemakers-users. The main reason why pacemakers are suitable for prophylactic replacement is the low variability in the device lifetime of batteries. The device life of VPs are depending on much more aspects causing unpredictable (early) VP leakage and a high variability in device lifetime. With problem-solving VPs, device life did become longer, but because of the high costs, they are not worldwide available for patients and when available mostly used in patients with short device lifetime [19,20]. Variability in device life is a problem found in all types and brands of VPs and different countries[16], making the results of this study generalizable for all patients using a VP, worldwide.

The ultimate goal in PVPR would be to replace VPs at a set moment (just) before leakage, predicted by previous device lifetime and known patient or treatment variables. With such a policy, one could reduce the number of unexpected VP replacements and potentially prevent aspirations. This would likely provide patients more security, peace of mind and possibly increase QoL. Planned replacements are also more convenient

for the treating physician or SLP. On the other hand, replacing VPs too early would implicate that patients need extra VPs and thus visit the clinics more often which would increase costs. The total costs of VPs and their replacements are very variable and depend on e.g., the type of VP used, hospital costs, number and type of healthcare professionals involved, travel expenses, and the healthcare system. Therefore, a costs analysis is not made.

Data on complications of leakage, such as aspiration pneumonia, was not available in our database, though they are important for decision-making in VP replacements. The review of Hutcheson et al. gives a nice overview of pneumonia rates in laryngectomized patients. They state that an aspiration pneumonia due to leakage is relatively rare, but it could have serious (fatal) consequences[21]. In Poland, there is an ongoing randomized controlled trial comparing the effect of replacement of VPs every three months to a Wait-to-Leak policy, investigating complications, fistula colonization, and patient satisfaction[22]. Results are not yet available. If their results show fewer leakages in the replacement arm and comparable or fewer complications and high patient satisfaction, this might be a step in prophylactic replacement of VPs.

Limitations

The concept of PVPR in this paper is hypothetical. Our results are based on analysis in a retrospective dataset and Monte-Carlo simulations, mainly investigating regular Provox VPs. It is well known that also other brands of VPs suffer from an inconsistent device lifetime[16], so it is unlikely that prophylactic replacement is an option for other brands. We have only investigated a cut-off point of 70%, because of reached consensus on the profitability for patients.

Conclusion

This is the first study exploring multiple policies to prevent voice prosthesis leakage using hypothetical prophylactic VP changes in laryngectomized patients. To prevent 70% of all occurred leakages during the study period, on average more than six additional VPs would be necessary annually per patient. The variability in device lifetime inter-, but most of all intrapatient, makes it impossible to predict device lifetime and set the interval for VP replacements. There are significant differences in device lifetime in subgroups for the used type of VP and indication for TL. These differences do not contribute to a better predictability of leakage. Based on the presented results prophylactic replacement of VPs is not a feasible policy.

Supplemental information

Monte-Carlo simulations of optimal time-to-change for voice prostheses

Monte-Carlo simulations of prophylactic voice prosthesis changes were performed with variable expected device lifetimes and variability in lifetimes. Simulations were done for different prophylactic replacement policies, comparing no-prophylactic device change (wait-to-leakage), to theoretical optimal replacement, adaptive replacement, initial best estimate, and fixed time replacement policies. Each simulated condition was run for 5000 simulated patients and 32 device changes. To investigate the influence of the Coefficient of Variation on expected time-to-leakage events and number of device changes in the ideal case of known probability distributions, time-to-leakage was simulated for 1 million device changes per data point. Results show that for the high variability in lifetimes found in the investigated patient population, Coefficient-of-Variation (Standard Dev. / Mean) > 0.8, no prophylactic device change policy will be effective in reducing the number of leakage events, even in the ideal case where the expected device lifetimes and Coefficient of Variations of individual patients are known.

The supplemental information contains the R and Rmarkdown code used in the simulations and the generation of the figures and text.

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Chapter 8

The Acceptance and Voice Quality of a New Voice Prosthesis "Vega High Performance" – A Feasibility Study

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Abstract

Background: The Provox Vega High Performance (PVHP) is a newly developed voice prosthesis (VP) with an aim to achieve a longer and more predictable lifetime.

Objectives: This feasibility study aims to assess patient acceptance of the PVHP VP, evaluate adverse events, voice quality, and device lifetime.

Methods: Laryngectomized patients previously using a Provox Vega or ActiValve Light were included. Acceptance and voice outcomes were evaluated at two time points with a two-week interval. Baseline measurements were taken with the standard VP, followed by placement of the PVHP for the two-week assessment.

Results: Fifteen participants completed the study, with thirteen being initial Vega-users. PVHP acceptance was 87% two weeks after placement. Median device lifetime for all VPs was 64 days (range 14-370). In the subgroup without periprosthetic leakage, the median device lifetime was 101 days (range 31-370). Acceptance dropped to 40% after device failure. Voice quality did not differ between PVHP and baseline VP. The most reported adverse event was PVHP valve stickiness (46%).

Conclusion and Significance: Acceptance of the PVHP is largely dependent on device lifetime, decreasing from 87% to 40% after leakage or replacement. Voice quality remains consistent across different VPs. Developing a long-lasting VP remains a challenge.

Keywords: Voice prosthesis, rehabilitation, laryngectomy, head-and-neck oncology

Introduction

After total laryngectomy (TL), restoration of voice is an essential goal of rehabilitation. Due to a more intelligible speech and better voice quality, trachea-esophageal speech (TES) using voice prostheses (VP) has become the gold standard in the Western World[1, 2].

VPs have a limited device lifetime and need to be replaced regularly, on average between two to six months, depending on the VP type[3, 4]. The most common reason for replacement is leakage through the VP due to malfunction of the valve, called transprosthetic leakage[5-8]. A major problem is that the device lifetime is unpredictable and varies enormously[9]. This leads to patients often experiencing issues with voice prostheses for which they need to visit a hospital, which demands a lot of healthcare workers[10]. Most patients use VPs such as the Provox Vega (Atos Medical AB, Hörby, Sweden) or the Blom-Singer Classic (InHealth Technologies, Carpinteria, CA). There are also problem-solving VPs available which can be used for problems such as underpressure, early leakage or fistula widening, causing periprosthetic leakage[11]. An example is the Provox ActiValve which has a valve made of fluoroplastic with a built-in magnet for optimal closure, and has proven to have a longer device lifetime (median > eleven months)[9, 11]. However, the ActiValve is costly in comparison to other VPs, and therefore not available for most patients due to reimbursement issues. A more affordable VP with a predictable and prolonged device lifetime would be of added value to the current market. Therefore, Atos Medical AB developed the Provox Vega High Performance (PVHP). The PVHP is made of silicon rubber with a fluoroplastic valve flap and valve seat, a material that resists biofilm destruction similar as in ActiValve[12], but without the use of a valve magnet. Fluoroplastic is a sticky material, for which the use of a lubricant is needed to prevent blockage of speech[13, 14].

The aim of this study was to investigate patient acceptance of the PVHP. Secondary outcomes were experienced stickiness of the valve, effort to speak, subjective and objective voice quality and device lifetime.

Material and methods

This is a prospective phase I clinical feasibility study performed at the Netherlands Cancer Institute (NKI-AvL) at the department Head-and-Neck Oncology and Surgery. The study was approved by their Medical Ethical Committee of the NKI-AvL (NL76694.031.21), and registered in Clinicaltrials.gov (NCT05079386). All participants signed informed consent before participating in this study.

Participants

Seventeen laryngectomized patients, >18 years, and initial baseline users of Provox ActiValve Light or Provox Vega (Atos Medical AB, Hörby, Sweden) (length 4, 6, 8, 10, 12.5, all 22.5 French diameter) were included in this study. Participants with current TEP problems, active recurrent or metastatic disease or unable to give informed consent were excluded.

Procedure and data collection

Between January 2022 until March 2022, patients who met the inclusion criteria were contacted for participation by telephone or during regular hospital visits.

The study consisted of a short- and long-term period assessment (see Figure 1). User acceptance was evaluated during an initial two-week period, with the option to participate in a long-term observation period of up to twelve months. It is expected that two weeks is long enough to evaluate short-term acceptance and short enough to replace the PVHP if the patient is not satisfied. The PVHP was replaced with their regular VP at the end of the study. Acceptance was re-evaluated after ending of the study.

Design of the PVHP

The PVHP is an indwelling voice prosthesis with an outer diameter of 22.5 French. The housing and valve hinge is molded in transparent silicone rubber, whereas the valve flap and valve seat are made of fluoroplastic, similar to the ActiValve. At the esophageal end of the shaft sits a valve unit consisting of a valve seat, hinge and valve flap (figure 2).

Use of the PVHP

After cleaning the PVHP in the morning, participants need to apply lubricant by putting a drop on a cleaning brush and rotating the brush in the VP. The lubricant is needed because of the stickiness of the fluoroplastic. The use of lubricant prevents the valve flap from getting stuck, which causes blockage of speech. This is also used by ActiValve-users and has been on the market since 2003 when the ActiValve was released. The lubricant is a medical grade silicone oil. This one drop should be enough to avoid excessive stickiness but can be reapplied if needed[13, 14].

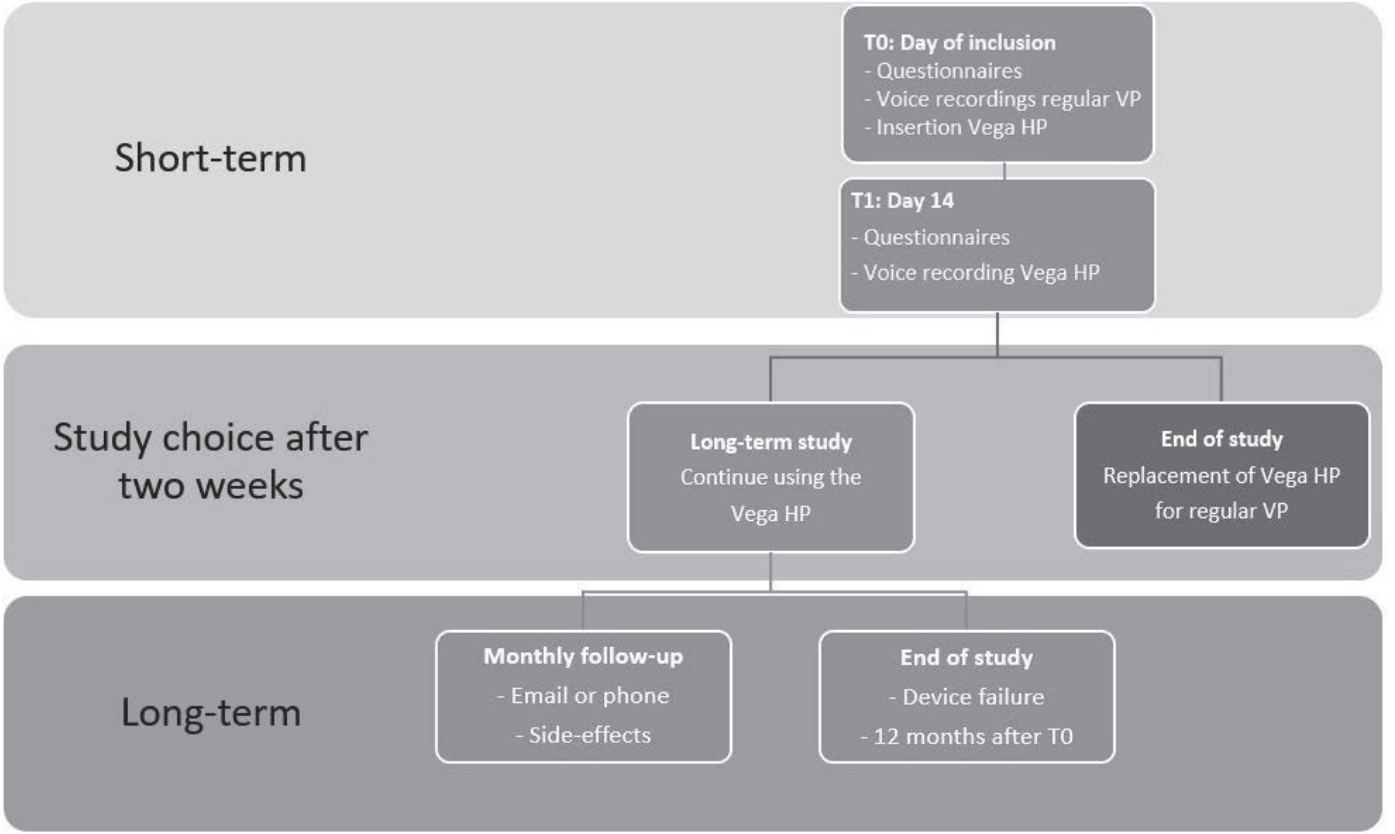

Figure 1. Flowchart of study design

Information regarding the used questionnaires can be found in the sections on primary and secondary outcome measures and appendix A

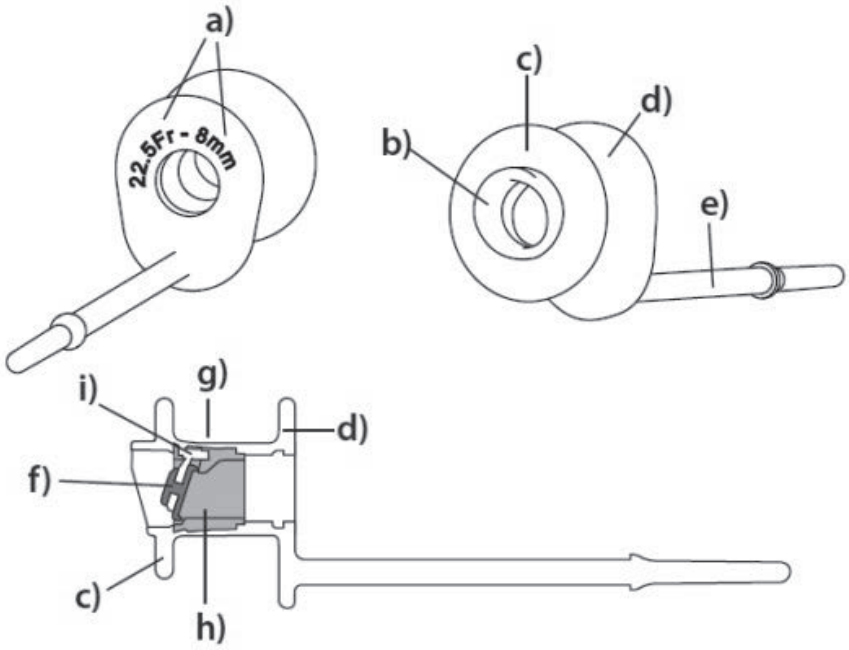

Figure 2. Schematics of the PVHP: a) Size information (shaft diameter and length between flanges) b) Prosthesis Hood c) Esophageal Flange d) Tracheal Flange e) Safety Strap f) Radio-opaque fluoroplastic Valve Flap g) Prosthesis Shaft h) Radio-opaque fluoroplastic Valve Seat i) Silicon Valve Hinge

Primary outcome measures

Participants' acceptance of the PVHP (primary endpoint) is measured with questionnaires, pre and two weeks post using the PVHP (see figure 1).

Questionnaires used (details in appendix A);

1) **Study specific questionnaires: Acceptance of the PVHP, experiences and maintenance of current VP, comparison of VPs.**
   Multiple choice questions about the experiences using the regular versus new VP, maintenance of the VP and possible side-effects (stickiness of the valve, voice quality, speech), acceptance and preference for a VP. Stickiness of the valve is evaluated in different ways, such as blockage of speech and problems with speech initiation.

2) **Voice Handicap Index – 10 (VHI-10)**
   The VHI-10 is a 10-item questionnaire to assess subjective voice quality. It contains ten statements and is used to assess subjective voice quality[15].

3) **Visual Analogue Scale Voice (VAS Voice)**
A VAS score for effort to speak, where 0 is the most effort to speak they could imagine, and 100 is the least effort to speak.

Voice evaluation
The Roland Edirol (Roland, Osaka, Japan) voice recorder was used for voice recording and assessment[16]. Voice recordings included reading aloud a text, producing a sustained /a/ at a normal pitch, and as low, high, soft and loud as possible. During both meetings questionnaires were filled in by the participant.

Secondary outcome measures
Voice recordings were analyzed and scored for intelligibility trough the objective Acoustic Voice Quality Index (AVQI) method[17]. The AVQI score gives a representation of the voice quality and is scored from 0-10. A score < 2.95 is considered as having a non-pathologic voice. Note: The AVQI is validated, but not for laryngectomized patients[18], but has shown to be useful to evaluate TE-speech[19].

Subjective voice quality and effort to speak ratings were done blinded by two experienced speech-language pathologists (SLP). Voice samples were scored from 0-10, where 0-5.5 is rated as not sufficient, 5.5-8 acceptable and 8-10 good. Maximum phonation time (MPT, in seconds) and loudness (loudest minus softest /a/ in dB, 90 and 50 percentile, respectively) are compared for both VPs.

Incidence and severity of reported problems and the comparison of the recorded voice assessments with their regular VP and PVHP are taken as secondary endpoints. Device life and leakage of VPs is noted.

Long-term study follow up
Subjects participating in the long-term study were monthly contacted regarding side-effects. This could be through calling, email or during a regular check-up in the hospital. After device failure the PVHPs the questionnaire regarding acceptance was filled in and the PVHPs were investigated for reasons of failure.

Statistical analyses
Statistical analysis of the collected data was performed with SPSS 27.0 (SPSS Inc., Chicago, IL, USA). Cross tabulations were used to compare the baseline and follow-up questionnaires. When suitable, the mean, median, standard deviations, range and variances of the analyzed data were visualized in tables. Because of the descriptive nature of this study, results were not tested for significance. The Two Way Mixed Intra-

class Correlation Coefficients (ICC) with absolute agreement and 95% confidence interval were used to determine the inter-rater reliability of the subjective voice assessments. This was done separately for the voice quality and effort to speak. An ICC of < 0 reflects 'poor', 0 to 0.20 'slight', 0.21 to 0.4 'fair', 0.41-0.60 'moderate', 0.61 to 0.8 'substantial' and above 0.81 'almost perfect'[20].

Device lifetime of the PVHP was calculated as day from insertion until device failure, or when no failure occurred in the twelve study months, until day of replacement.

Results

Patient characteristics

Of the seventeen included patients, we had one immediate drop-out. After placement of the PVHP he changed his mind and did not feel comfortable with trying a new VP. During the short-term study one patient was diagnosed with metastatic disease after which he was excluded. This left us with fifteen patients for analysis (figure 3). All patient characteristics are shown in Table 1. The majority of the participants were male, participants had a mean age of 71 years at start of the study.

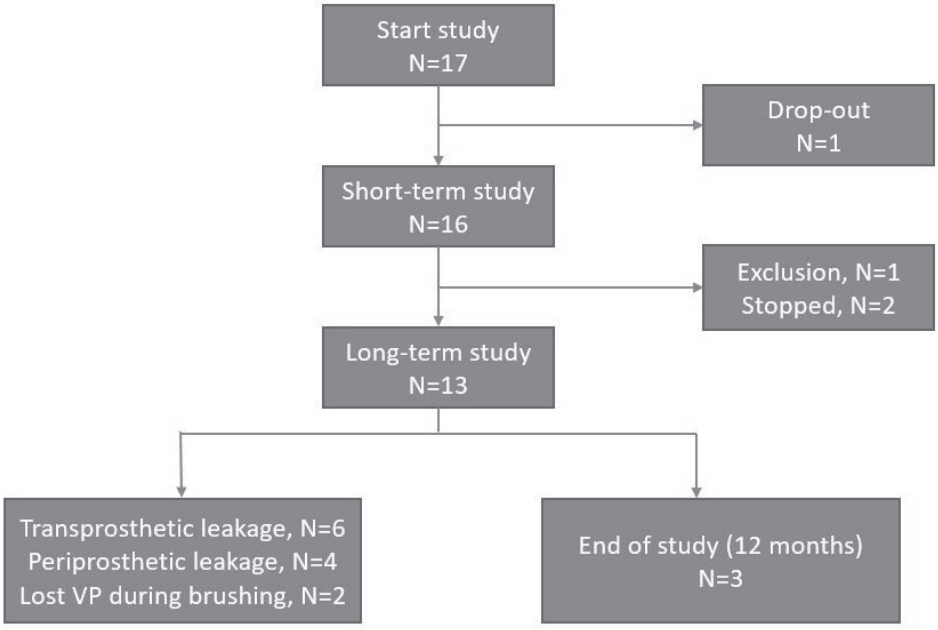

Figure 3. Flow diagram of included patients and study progression

Table 1. Patient, tumor, and treatment characteristics (n = 15)

Characteristics		N %
Gender	Male	12 80
	Female	3 20
Age	Mean, range	71.7 57-80
Time since TL in years	Mean, range	11.1, 0.3-43.4
Tumor-stage	I	2 13.3
	II	6 40.0
	III	1 6.7
	IV	3 20.0
	Unknown	3 20.0
Primary tumor site	Larynx	13 86.7
	Hypopharynx	2 13.3
Indication TL	Primary TL	3 20.0
	TL for recurrence	5 33.3
	Dysfunctional larynx	2 13.3
	TL for second primary tumor*	5 33.3
Pharyngectomy	No (standard laryngectomy)	10 66.7
	Yes, (all total pharyngectomy)	3 20.0
	Unknown	2 13.3
Neck dissection during TL	No	5 33.3
	Unilateral	3 20.0
	Bilateral	6 40.0
	Unknown	1 6.7
Reconstruction	No (primary closure)	6 40.0
	Yes	7 46.7
	Unknown	2 13.3
Radiotherapy	No	1 6.7
	Primary	11 73.3
	Postoperative	3 20.0
Chemotherapy	No	14 93.3
	Postoperative	1 6.7

*Other primary tumors were: upper esophagus (n=1), hypopharynx (n=3) and, oropharynx (n=1).

Regular voice prosthesis

Twelve patients (80%) used a Vega as their regular VP, and three (20%) an ActiValve Light. The median device lifetime of the whole group their previous VP was 113 days (range 7-427). For the ActiValve-users this was median 94.5 days (mean 133, range 7-357) and for Vega 117 days (mean 119 days, range 12-427). The main reason for replacement was transprosthetic leakage (N=12).

Acceptance of the PVHP

After two weeks (short-term follow-up) thirteen (86.7%) participants accepted the PVHP, of which nine (60%) preferred the PVHP over their regular VP because of experiencing an improved voice and less effort to speak. Five patients experienced increased stickiness of the valve flap when using the PVHP compared to two patients with their regular VP, regardless of the regular type of VP used. None of the patients reported the daily use of lubricant as a negative aspect.

Short-term follow-up

None of the patients decided to replace the PVHP before the end of the short-term follow-up. Two patients (2/15: 13%) had periprosthetic leakage during these two weeks, which was the reason to not participate in the long-term study. One of them is familiar with a short device lifetime (previous device lifetimes were 7 and 15 days).

Subjective voice quality and adverse events (study-specific)

Seven of the fifteen patients (46%) reported a better voice quality with the PVHP, four (27%) with their regular VP and the remaining four (27%) noticed no difference. These seven patients (46%) also reported less effort to speak when using the PVHP, four (27%) when using their regular VP and four (27%) reported no differences. Two (13%) of the patients reported less stickiness of the valve flap with the PVHP (one ActiValve and one Vega User), three (20%) reported no difference between the VPs (one ActiValve and two Vega users) and ten (67%) reported less stickiness with their regular VP. Ten (67%) patients reported disadvantages of the PVHP, which were blocking of speech and stickiness of the valve flap (n=7, 46%), leakage (n=4, 27%) and, excessive mucus production (n=2, 13%).

Net promotor score

A median score of 7 was reached (range of 0-9). Ten (67%) participants would recommend the PVHP to other patients, and five (33%) would not.

Voice Handicap Index -10

Nine (60%) patients had a VHI-10 score of 11 or higher when using their regular VP (a score above 11 is considered as limiting in daily life). This number increased to 12 (80%) when using the PVHP. The median VHI-10 score of the regular VPs was 14 (range 4-32 in comparison to 21 (3-35 for the PVHP. When comparing differences within subjects, eight (53%) patients scored higher with the PVHP than with their regular VP, one (7%) had comparable scores for both VPs, and six (40%) scored better with their regular VP (see figure 4A).

AVQI score

As shown in figure 4B, all participants have a higher score (meaning a deviant voice) than the cutoff point (2.95, red line). The median AVQI score of the PVHP was 8.4 (range 7.05-10) and 8.2 (range 6.93-10) for the regular VP.

Voice Quality and Effort to speak (rated by SLPs)

Fourteen voice recordings could be analyzed since one of the participants was not able to speak at the first meeting (participant 9). The inter-rater reliability (ICC) of the subjective voice assessments was 'almost perfect' for the effort to speak (0.933, 95% IC 0.856-0.969) and 'substantial' to 'almost perfect' for the voice quality (0.863, 95% CI 0.707-0.937). The mean effort to speak and voice quality scores were worse for the PVHP in comparison to the regular VP. The voice quality rating decreased from 5.1 (regular VP) to 4.4 (PVHP) and the effort to speak rating decreased from 3.7 (regular VP) to 3.0 (PVHP). Six (43%) patients had better voice quality with the PVHP compared to with their regular VP, and eight (57%) were rated with better voice quality with their regular VP. Seven (50%) needed less effort to speak with the PVHP, and seven (50%) less with their regular VP. See figure 4C and 4D for individual scores.

The maximum phonation time (MPT) with their regular VP was median 4.60 seconds (range 1.90-27.74), and with the PVHP median 5.37 seconds (range 0.98-22.79). The loudness with their regular VP was median 4.65 dB (range 2.8-11.0) and for the PVHP median 5.1 dB (range 1.6-10.8).

Long-term follow-up

Device lifetime

To determine device lifetime, data of all fifteen participants was analyzed (see table 2). Ten subjects (67%) had their PVHP replaced because of leakage (transprosthetic n=6, periprosthetic n=4). Three participants (20%) had the PVHP replaced because of reaching the one year follow-up without device failure/leakage. Noteworthy is that two subjects (13%) brushed the PVHP out of their stoma without need for medical

intervention, except for a replacement. The median device lifetime of the whole group was 64 days (mean 120 days, range 14-370). Upon exclusion of the VPs with periprosthetic leakage and the VPs that were brushed out, the median device lifetime was 101 days for this subgroup (mean 167, range 26-370). See figure 5.

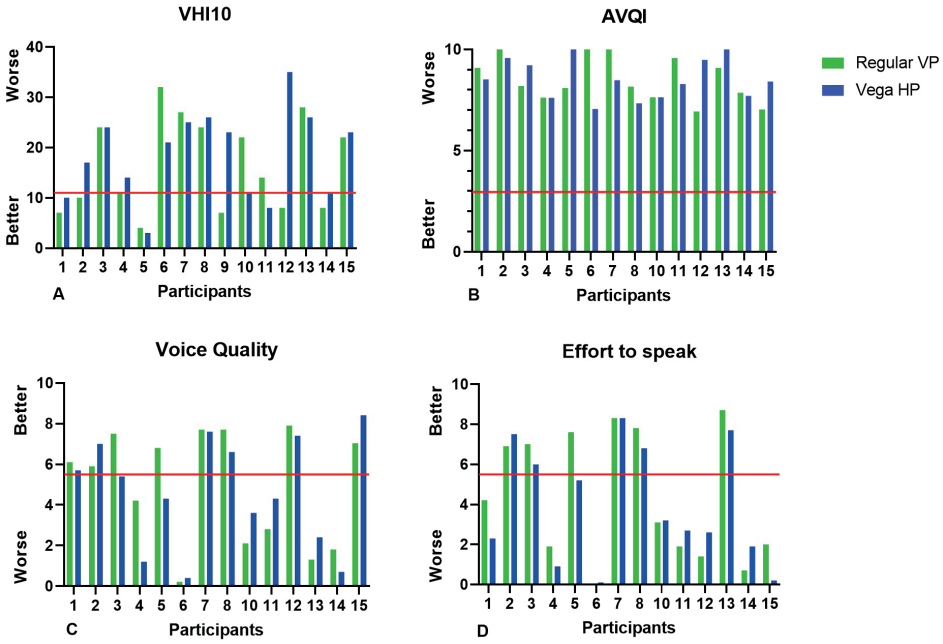

Figure 4. Overview of subjective and objective voice outcomes

A: VHI10 scores, range 0-40. A score above 11 points (red line) is considered as having an abnormal voice, which is subjective limiting in daily life.

B: AVQI scores, range 0-10. The lower the score, the better the voice. A score < 2.95 (red line) is considered as having a healthy voice.

C: Voice quality as rated by SLPs, range 0-10. A score <5.5 is rated as poor/pathologic.

D: Effort to speak as rated by SLPs, range 0-10. A score <5.5 is rated as too much.

The trade-off question showed that the minimum desired device life of the PVHP, to outweigh disadvantages, was median six months (range three to twelve months). During the long-term study period there were no new adverse events reported.

Table 2. Device lifetime of the PVHP

Subject	Device lifetime (days)	Reason for replacement	Visual inspection VP	Acceptance after ending study
1	31	Transprosthetic leakage	Biofilm formed on silicone parts. Small leakage detected.	No
2	101	Transprosthetic leakage	Some residues on sealing surface that came off after cleaning. No leakage detected.	No
3	120	Transprosthetic leakage	Fungus ingrowth on all silicone surfaces exposed to the esophageal side. Small leakage detected.	**Yes**
4	27	Lost VP during brushing	No damages or leakage detected	No
5	52	Transprosthetic leakage	Residue on sealing surface	No
6	370	End of study	Residues on sealing surface. Small leakage detected.	**Yes**
7	26	Transprosthetic leakage	Difficult to clean, residues on sealing surface close to hinge. Small leakage detected.	No
8	64	Periprosthetic leakage	Residues on sealing surface that came off after cleaning. No leakage detected.	No
9 §	22	Periprosthetic leakage	No damages or anomalies	No
10	151	Lost VP during brushing	N/a	**Yes, but prefers ActiValve Light**
11	367	End of study	Residues on sealing surface. Small leakage detected.	**Yes**
12 §	14	Periprosthetic leakage	Biofilm on silicone parts.	No
13	91	Transprosthetic leakage	VP not returned	**Yes**
14	343	End of study	Small leakage detected. Leakage stopped after cleaning	**Yes**
15	27	Periprosthetic leakage	Residues on sealing surface that came off after cleaning. No leakage detected.	No

§ Did not participate in long-term study

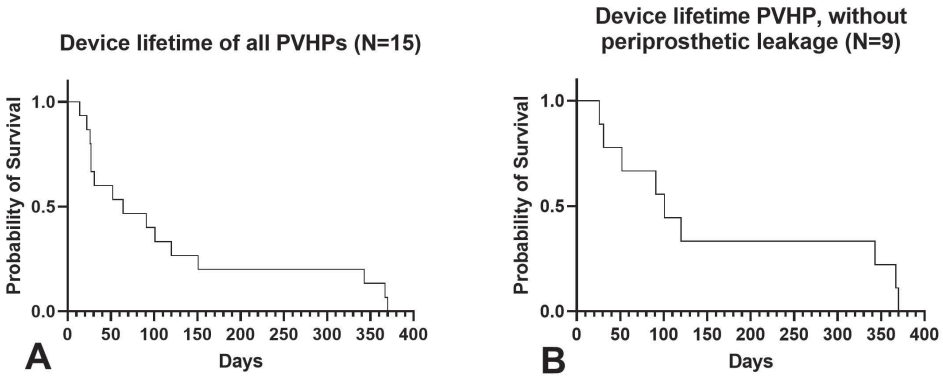

Figure 5. Kaplan Meier curve of the Device lifetime of the PVHP

A: The whole group (n=15), B: Without periprosthetic leakage and lost VPs (n=9)

Acceptance after ending study

Two participants did not accept the PVHP due to early leakage. Of the remaining thirteen participants who continued in the long-term phase, six participants accepted the PVHP but one of them preferred the ActiValve Light because of the experienced longer device lifetime. The remaining seven did not accept the PVHP because of the relatively short device lifetime. In total six out of fifteen participants (40%) accepted the PVHP after ending the study (see table 2 and figure 6).

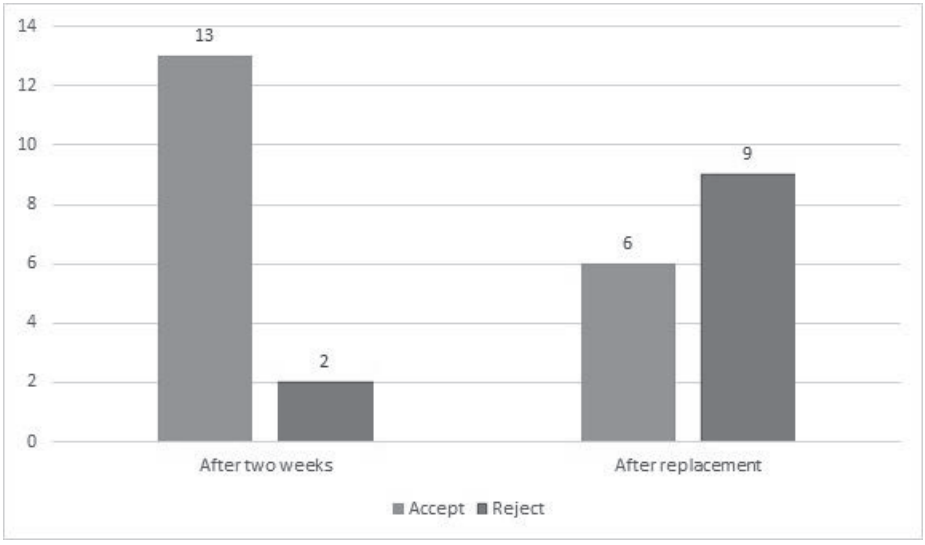

Figure 6. Overview of acceptance of the PVHP at two time points

Discussion

This feasibility study found that the short-term acceptance of a newly developed voice prosthesis called 'PVHP' was 87%; however, it dropped to 40% after replacement of the PVHP due to device failure. Acceptance is a composed outcome measure, in this study, depending on factors related to the patient, but also on other outcomes such as stickiness of the valve, speech and device lifetime. The difference in acceptance rate at these two time points (short-term versus long-term follow-up) can mainly be explained by the shorter than anticipated device life.

The most reported side-effect was blocking of speech due to stickiness of the valve, which is caused by the used material and is a well-known side-effect of the ActiValve, made from the same material[11]. All patients were able to solve these problems by coughing, brushing the VP and/or reapplying lubrication. ActiValve-users were common with lubricating and thus reported less side-effects compared to the Vega-users. The use of lubrication was not considered a main issue, comparable with the ActiValve[11, 13].

Surprising, half of the patients rated their voice quality and effort to speak better with the PVHP compared to their regular VP, which was not found by the blinded perceptual evaluations of the SLPs. This could be the effect of the 'take-the-best heuristic', where people assume "new is better", and score new products initially better than they perform[21].

Looking at the results of the VHI-10, only two participants rated their voice as normal and not limiting during daily life, all the others rated their voice as a handicap. This finding is comparable with other publications[2, 19]. The AVQI is an objective acoustic outcome measure. The mean AVQI score was the same for the regular and new VP (8.5), which means that all participants had a distorted voice quality (score > 2.5). It is clearly visible that patients rate their voice quality better than the objective scoring, and there are no differences between the types of VP[22]. As none of the objective scorings are validated for TE speech, AVQI scores have to be interpreted carefully[19, 23]. When looking at the maximum phonation time and loudness, we saw that both were slightly better with the PVHP compared to the regular VP.

Device lifetime varies enormously, both inter- and intra-patient and seems to be very multifactorial[9]. Although this study is not powered to assess a realistic device lifetime, the device lifetime of the PVHP in this pilot was relatively short (median 64 days). This is inferior to the device lifetime of the ActiValve (165 days)[11], but comparable with the Provox2 (63 days), Provox Vega (66 days)[3] and the Blom-Singer Classic (69 days)[4]. The

concept of a fluoroplastic valve flap and valve seat was expected to prevent biofilm formation and therefore a longer device lifetime. The main reason for leakage however seems to be food residue on the valve or valve seat. However this needs further study as this is not investigated before in other VPs. This study indirectly confirms that the magnet in the ActiValves are probably the key component in their longer device lifetime[13].

Our cohort included two patients that displaced their PVHP due to brushing. Despite the fact that brushing and lubricant are widely used in VPs such as the ActiValve[13, 14], the percentage of such displacements in our clinic, and also in the literature is unknown. One of the two participants has a relatively wide and fragile tracheo-oesophageal fistula, which could potentially be the underlying cause of displacement. For the other participant the cause of the brush-out remains unclear.

Investigating and developing new voice prostheses is quite challenging due to the small number of laryngectomized patients and multifactorial issues determining device lifetime. In vitro research of VPs has shown to be useful for investigating the composition and prevention of biofilm formation[24, 25]. But this leaves out all other factors, such as cleaning of the VP, diet, reflux, pressure in neopharynx and stoma problems. To investigate the quality and device lifetime of a VP, a large cohort of patient is needed to give a valid overview of the device lifetime in vivo. The search for a new voice prosthesis with a longer device lifetime is needed to improve patient acceptance and increase quality of life for these patients, but this remains a great challenge.

Limitations

This is a feasibility study, investigating acceptance of a new voice prosthesis, and only the rating of the voice recordings was blinded. It was not powered in finding differences between VPs. Due to the limited sample size it is hard to draw definitive conclusions on voice quality and device lifetime. Acceptance of a voice prosthesis is a complex outcome measure associated with many other factors such as stickiness of the valve flap and device lifetime.

Conclusion

This feasibility study of the new voice prosthesis 'PVHP', showed that the patient acceptance was 40% (6/15). Patient acceptance seems to depend on device lifetime rather than side effects such as stickiness of the valve and the use of lubricant. The device lifetime was relatively short (median 64 days) and therefore the main limiting factor in acceptance by patients. Subjective and objective voice ratings did not show differences between the regularly used VP and the PVHP. The search for an affordable new voice prosthesis with a long device lifetime remains a complicated challenge.

Appendix A

Additional information regarding used questionnaires

1) Study specific questionnaires: Acceptance of the PVHP, experiences and maintenance of current VP, comparison of VPs.
   Multiple-choice questions about the experiences using the regular and new VP (stickiness, voice quality and speech), maintenance of the VP and possible Adverse Events, Adverse Device Effects or Device Deficiency. The acceptance of the PVHP and preference for type of VP is asked at the end of the short-term study as well as after leakage or wearing the VP for twelve months. Part of this questionnaire is the Net promotor score[26] (the probability that participants will recommend the new VP to others on a visual analog scale (VAS) from 0-10). There is a trade-off question regarding the minimal desired device lifetime to outweigh possible experienced adverse events, and there are comparative questions for experiences for speech/voice, effort to speak, stickiness of the VP valve, leakage, cleaning of the VP.

2) Voice Handicap Index – 10 (VHI-10)
   The VHI-10 is a 10-item questionnaire to assess subjective voice quality. It contains ten statements and is used to assess subjective voice quality. Each statement has five answer options: never, almost never, sometimes, usually, and always. A score above 11 points is considered as having an abnormal voice, limiting daily life activities (range 0-40 points)[15]. The VHI-10 is often used, but not validated for laryngectomized patients[19, 27]

3) Visual Analogue Scale Voice (Vas Voice)
   With help of a VAS score, effort to speak is measured. In this score, 0 is the most effort to speak they could imagine, and 100 is the least effort to speak. A VAS is a measurement instrument that tries to measure a characteristic or attitude that is believed to range across a continuum of values and cannot easily be directly measured, most used for pain[28]. This VAS score gives a representation of the effort to speak.

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Chapter 9

Maximal Cardiopulmonary Exercise Testing in Laryngectomized Patients using Different HMEs – Feasibility and Exercise Responses

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Abstract

Objective After laryngectomy, breathing resistance of Heat-and-Moisture-Exchangers (HMEs) may limit exercise capacity. Breathing-gas-analysis during cardiopulmonary exercise testing (CPET) is not possible using regular masks. We tested the feasibility of CPET with an HME in situ, using an in-house designed connector. Additionally, we explored the effect of different HME resistances on exercise capacity in this group.

Methods Ten participants underwent two CPETs using their daily life HME (0.6 or 0.3 hPa) and one specifically developed for activity (0.15 hPa). HME order was randomized and blinded.

Results All participants completed both tests. No (serious) adverse events occurred. Only 4 subjects reached a Respiratory Exchange Ratio RER>1.1 in at least one test. Maximum exercise levels using HMEs with different resistances did not differ.

Conclusion CPET in laryngectomees with an HME is feasible, however the protocol does not seem appropriate to reach this group's maximal exercise capacity. Lowering HME resistance does not increase exercise capacity in this sample.

Keywords: Laryngectomy, exercise training, Head and Neck Cancer

Introduction

A total laryngectomy (TL) is performed as primary treatment for advanced stages of laryngeal and hypopharyngeal carcinomas or as a salvage treatment. As TL separates the upper and lower respiratory tracts, air no longer passes through the upper airways. Instead, air is inhaled through a stoma in the neck, where it immediately enters the lower airways [1,2]. The upper airway heats, humidifies and filters inhaled air. After a laryngectomy, these functions are lost. As a result, patients experience increased pulmonary symptoms, such as involuntary coughing, mucus retention, and a need for forced expectoration to clear the airways[3,4]. Additionally, patients have a higher risk of infection and inflammation of the airways [5,6]. These airway problems significantly influence sleep, social contacts and quality of life[7].

Stoma cloth covers (bibs) and Heat and Moisture Exchangers (HMEs) have been developed to restore some of these lost functions. Bibs are worn in front of the stoma. They can provide a good level of heating and moisturizing of the inhaled air when worn correctly, and are reusable and inexpensive[8]. On the downside, bibs give difficulty in occluding the stoma to speak, have a high breathing resistance and are usually not preferred by patients. Therefore, HMEs are the preferred devices in most developed countries[9]. HMEs are placed in an adhesive baseplate which is placed over the patient's stoma or in a canula. The device passively retains the heat and moisture from expired air, which is then transferred to the inhaled air of the next breath[10–12]. HMEs improve the tracheal climate, resulting in less involuntary coughing and less sputum production[11]. Long-term use of HMEs has shown to prevent and even restore the loss of tracheal ciliated cells and improve quality of life[12]. The size of the HME as well as the internal pore sizes and salt concentration determine the performance and resistance of an HME[13,14]. HMEs worn in front of a stoma have limited space and size. As a consequence, there is always a compromise between efficacy/performance of and HME and its resistance. HME resistance has been reported as a limiting factor for compliance (continuous use of HME) and might cause discomfort during physical activity, when ventilation demand increases[11]. Such discomfort contributes to lower levels of HME compliance and may cause patients to avoid physical activity or exercise. This, in turn, can lead to poorer overall health and fitness as well as a lower quality of life[15].

There are multiple HMEs available, with different levels of resistance and humidification, aiming to serve specific purposes such as higher filtration of (polluted) air or enhancing suitability for physical activities. In general, it is accepted that better HME's (with higher resistance), and high compliance (wearing them 24/7) have a positive effect

on symptoms and quality of life[16]. Aside from differences in experienced comfort, it is currently unknown to what extent differences in HME resistance influence acute exercise responses, and exercise capacity and performance.

To understand the differences between HMEs in terms of their impact on exercise tolerance and exercise response, exercise testing is required. The gold standard for cardiopulmonary exercise testing is a maximal Cardiopulmonary Exercise Test (CPET) with breathing gas analysis[17–19]. In patients after TL, this is complicated since the regular facial masks used for breathing gas analysis cannot be used. Previously, exercise testing using a custom-made adapter attached to the base plate of the HME, but without the HME being in-place, proved to be feasible[20,21]. However, this approach discards the effect of the HME on upper airway physiology. In addition, it creates an unnatural situation for patients, which may impact the results of exercise testing.

To enable research into the impact of an HME's resistance on exercise capacity, we developed an adapter that allows exercise testing with the HME in situ. In this exploratory study, we tested the feasibility of this set-up for CPET in ten laryngectomized patients and explored the influence of HME resistance on their exercise capacity and performance.

Materials and Methods

Participants

Ten subjects were included, using convenience sampling from the outpatient pool of the department of Head-and-Neck Oncology and Surgery at the Netherlands Cancer Institute. All had undergone a total laryngectomy (TL) and were at least six months postoperative. Inclusion criteria were: fully independent in activities of daily living (ADL), and regular self-reported participation in moderate-intensity leisure physical activities (>30 minutes), three or more times a week. A history of cardiac problems[22] (such as unstable angina, arrhythmias, myocardial infarction, syncope), and active oncological disease were exclusion criteria. All patients were daily HME users (Provox® Life™, Home or Go, Atos Medical AB, Hörby, Sweden).

HMEs

All subjects were tested twice to allow comparison of exercise capacity and performance between HMEs with different resistance properties. Patients used their regular HME, which could be either the Provox® Life™ Home or Go, in one of the tests, and a lower resistance HME: the Provox® Life™ Energy HME (Atos Medical AB), specifically developed for use during physical activity, in the other. HME specifications for resistance and moisture loss of each of the HMEs used in the study can be seen in table 1.

Table 1. HME Specifications*

	Flow Resistance	Moisture Loss
Energy HME	0.15 hPa	23.0 mg/l
Go HME	0.30 hPa	22.5 mg/l
Home HME	0.60 hPa	19.5 mg/l

This technical data comes from the instructions of use of the products. Flow resistance is measured as 30L/min(Pa)

3D-printed connector for CPET

To replace the regular facial masks used for breathing gas analysis, an in-house 3D printed adapter was developed, which can be connected to the adhesive baseplate in front of the tracheostoma, with the HME in place. The connector was designed in such a way the HME is not visible to the patient once placed and closed, enabling blinding during testing. The breathing-gas-analysis was corrected for the additional dead space of the connector (78,68 ml). Picture 1 gives an overview of the connector and where the HME is placed in the connector. The connector is made out of polyamide 12 (Oceanz PA12)[23] and can be cleaned by washing it with water and soap and rinsing it with disinfectant (70% alcohol).

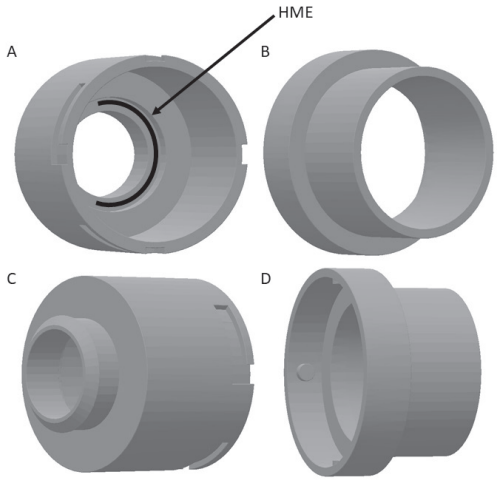

Figure 1. The 3D-printed connector

A: The inside of the connector, the arrow shows where the HME is placed. A and C: This part is connected to the patient's stoma by placing it into the adhesive baseplate.

B and D: This part is connected to the computer for breathing gas-analysis. As visible in C and D: the two parts can by connected by sliding and locking it.

Study design

Participants were randomized into two groups (1:1) using opaque envelopes, which determined the order of the HMEs to be used during CPET-testing. During the test, patients were blinded to the HME in use, which was installed in the 3D-printed connector (Figure 1) by the researcher administering the test (Anne Heirman).

Exercise Testing Protocol

CPETs were conducted on two separate visits, with two weeks in between. The tests were performed using an electronically braked cycle ergometer (Lode Corival, ProCare, Groningen, The Netherlands). Throughout testing, the subject's heart rate was continuously monitored with a 12-lead Electrocardiogram (ECG). Breathing-gas-analysis was carried out with a calibrated ergospirometry system (Jaeger Masterscreen CPX, Houten, The Netherlands). Directly after finishing the test, participants were asked to rate their perceived level of exertion and dyspnea, on a Borg scale ranging from 6-20, with 20 indicating maximal exertion[24]. Prior to testing, there was a five-minute period of slow pedaling so subjects could familiarize themselves with the bicycle. The test started with three minutes of unloaded cycling followed by an increase in load every minute until subjects could no longer maintain the desired cadence (between 60 and 80 RPM). The load was increased by 15 or 20 watts per minute, based on the

participant's estimated fitness level[25]. Patients were encouraged to push themselves maximally during the CPET. Indications for terminating CPET were chest pain, ischemic ECG changes, sudden pallor, signs of respiratory failure, and patients' wish to stop. Before the test, it was explained to patients that symptoms such as muscle fatigue and exhaustion are not reasons for stopping, but normal responses to the effort on the CPET. VO_2 peak was obtained by taking the average value over the last 30 seconds of the exercise test. Anaerobic threshold was determined by using the V-slope method[26]. The two exercise tests were conducted with the same test protocol and under similar testing conditions, with the only difference being the HME in use. See figure 2 for the study set-up with a patient during CPET.

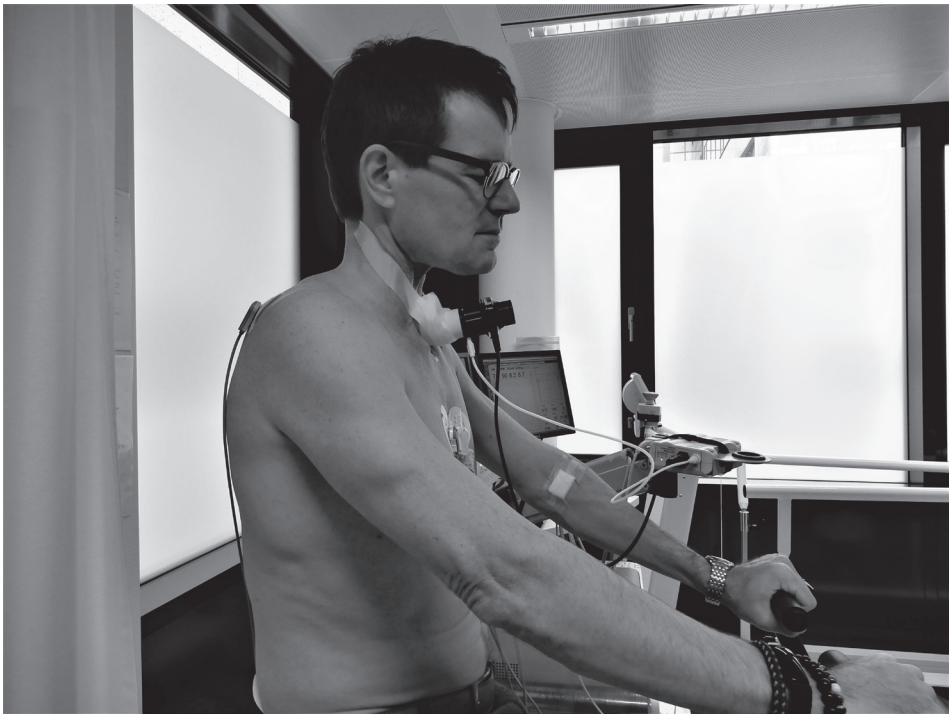

Figure 2. CPET set-up. A study participant* connected to a breathing gas analyzer while seated on the exercise bicycle. *The participant gave permission to use his picture in this article, see signed contract appendix A

Feasibility criteria

To explore the feasibility of this CPET set-up in laryngectomized patients, a priori criteria were set, based on literature and consensus in the research team, each of which had to be satisfied:

1. The connector is not leaking air during the measurements
2. Subjects are not complaining about discomfort using the connector with an adhesive baseplate and HME
3. No occurrence of (serious) adverse events, such as hyperventilation, dyspnea, ECG abnormalities, collapse, etc.
4. At least 80% of the patients are able to reach a Respiratory Exchange Ratio*>1.1 (RER=VCO2/VO2) and/or 95% of their predicted maximum heart rate in at least one of the tests[27,28]

** Respiratory exchange ratio (RER) = the ratio between the metabolic production of carbon dioxide (VCO_2) and the uptake of oxygen (VO_2)*

Data from CPET

Variables of interest were Time in Test, Peak Workload (Wpeak), Heart Rate (heartbeats per minute), Perceived level of exertion (Borg-score; score ranges from 6 till 20 in which a higher score resembles a higher perceived effort), peak oxygen uptake (VO_2 peak) both absolute (L/min) and relative to body weight (ml/kg/min), RER, anaerobic threshold (VO_2/kg) and ventilatory efficiency expressed as minute ventilation/carbon dioxide production at anaerobic threshold (VE/VCO_2).

All data were calculated for the total group as well as for the subgroups based on regularly used HME type (0.3 or 0.6 hPa), and HME used during the test (regular or lowest resistance). We used graphs to plot outcomes for the 0.15 hPa HME (Energy) against those obtained with patients' regular (Go or Home) HME.

Statistical analysis

All data was analyzed using IBM SPSS statistics 27 and Graphpad Prism 9. Since this was an exploratory study with a small sample size, we did not statistically test the differences for significance, but rather provide descriptive analyses and visual displays of patient data.

Ethical considerations

The authors declare that all procedures contributing to this work are performed in accordance with the ethical standards of the medical ethical review committee of the Netherlands Cancer Institute who approved the study (registration nr. NL72840.031.20), and with the Helsinki Declaration of 1975, as revised in 2008.

Results

Subjects

Nine (out of ten) patients were male, and six of them had been treated with (chemo) radiotherapy before TL. One participant had asthma, not limiting in daily life activities and sports. None of the other participants were diagnosed with pulmonary diseases. All patients were former smokers but had stopped since treatment. For further patient and treatment characteristics, see Table 2.

Feasibility of CPET

None of the ten patients experienced air leakage through the connector and/or adhesive baseplate, and there were no abnormalities in the results from the breathing gas analysis. All patients were comfortable wearing the connector, there were no complaints of discomfort or dyspnea, and no (serious) adverse events occurred during the CPETs or in the following days. So, all first three feasibility criteria were met. Feasibility criterion four was not met. An RER>1.1 was reached by four patients, of which two in the first test and two in the second (all with the 0.6 hPa HME), while only two patients reached it in both tests. Only one subject reached 95% of his maximum predicted heart rate in one test. This was the test with his regular 0.6 hPa HME. See Table 3 and 4 for more details.

Overall CPET results

The overall average time in test was 958.5 seconds, with a median Wpeak of 126 Watts (range 39-254), and a median VO_2peak of 1.55 L/minute (range 1.07-2.71), over all CPETs conducted. Median VO_2 peak for patients reaching RER>1.1 was 1.85 L/minute (1.33-2.71). Under all testing conditions (see table 3), we observed normal responses to exercise for heart rate (HR), oxygen consumption (VO_2), ventilatory efficiency (VE/VCO_2), minute ventilation (VE), and respiratory exchange ratio. On average, relative VO_2peak was quite low, especially for the regular 0.3 hPa HME users. Regular 0.6 hPa HME users (n=8) performed better compared to regular 0.3 hPa HME users (n=2) in this sample: they cycled longer, achieved higher workloads, and higher peak values. When comparing the CPET results obtained with the regular HME to those obtained using the lowest resistance HME, we observed no meaningful differences. For seven patients, their anaerobic threshold (AT) could be determined, see table 4. For two patients (8 and 9), the AT could not be determined, while one subject (3) did not reach the AT in both tests because of subjective exhaustion and feeling out of breath. Only one subject reached his 95% predicted heart rate, in the test with his regular resistance (0.6 hPa).

Table 2. Patient and treatment characteristics

	N=10
Age in years (mean, range)	63.6, 49-79
Gender	
Male	9
Female	1
Time since TL in years (mean, range)	10.7, 1-30
Primary tumor	
Larynx	9
Hypopharynx	1
Prior treatment	
RT/CRT	5/1
Vertical hemi-laryngectomy	1
None	3
Adjuvant treatment	
RT	2
None	8
Neck dissection	
Bilateral	5
None	5
Flap reconstruction	
PM	2
SCAIF	1
None/unknown*	7
Pulmonary disease(s)	
None	8
Asthma	1
Pulmonary Embolism**	1
History of smoking	
Former	10
No	0
Daily type of HME	
Home	8
Go	2

CRT = chemo-radiotherapy, RT = radiotherapy, PM = Pectoralis Major flap, SCAIF = Supraclavicular Artery Island Flap

* No report available ** Pulmonary embolism in 2012

Table 3. Median values at the end of CPET

	Regular resistance			Lower resistance (0.15 hPa)		
	Total group N=10	0.6 hPa N=8	0.3 hPa N=2	Total group N=10	Usual 0.6 hPa N=8	Usual 0.3 hPa N=2
Time in Test (seconds)	**1000**	1006	930	**999**	1000	916
Wpeak (Watts)	**141.2**	148.1	101.0	**129.7**	136.2	90.0
HR (beats per minute)	**138**	138	134	**133**	133	131
VO_2peak (L/min)	**1.48**	1.62	1.04	**1.59**	1.72	1.14
Relative VO_2peak (ml/kg/min)	**20.4**	21.4	15.7	**20.6**	21.9	15.8
VE peak (L/min)	**57.1**	61.2	42.0	**53.0**	56.2	45.0
RER	**1.05**	1.10	0.85	**1.00**	1.05	0.91
Anaerobic threshold* (VO_2/kg)	N=7	N=6	N=1	N=7	N=6	N=1
	12.4	12.0	17.6	**12.0**	11.4	13.6
VE/VCO_2 at anaerobic threshold	**32.4**	31.9	38.7	**33.2**	32.4	34.2
Borg-Score Min score 6; low effort – max 20; high effort)	**15.0**	15	16.0	**14**	14	16.5

All scores are medians. Total group scores are displayed in bold. Individual scores and therefore ranges can be found in Table 4. *Anaerobic threshold was not reached by 1 subject and could not be determined in two subjects (see table 4 for details). Abbreviations: maximum workload (Wpeak), heart rate (HR), maximum oxygen consumption (VO_2 peak), CO_2 production (VCO_2), respiratory exchange ratio (RER), and minute ventilation/carbon dioxide production at anaerobic threshold (VE/VCO_2).

Wpeak and VO_2peak related to resistance level

Figure 3 shows the comparisons of individual results per test. As can be seen from the graphs, patients performed quite similarly in both tests, regardless of HME worn. The results for Peak oxygen consumption (VO_2peak, graph 1B) show more variability between the two resistances compared to other outcomes, but are still quite similar and within limits of regular test-retest variability[29].

Table 4. Individual results of CPET

Subject	RER Regular resistance		Wpeak	VO_2 peak †	HR	Termination reason
	0.3 hPa	0.6 hPa				
1	n/a	0.96	99	1.11	114	Leg fatigue and out of breath
2	n/a	1.06	129	1.62	136	Exhaustion
3 *	0.73	n/a	75	1.07	114	Leg fatigue and out of breath
4	n/a	**1.27**	254	2.71	**171**	Exhaustion
5	n/a	**1.16**	170	1.88	127	Exhaustion
6	n/a	**1.10**	108	1.33	141	Exhaustion
7	1.04	n/a	126	1.36	150	Dyspnea and exhaustion
8 **	n/a	1.06	69	1.31	148	Out of breath and exhaustion
9**	n/a	0.98	150	1.96	133	Leg fatigue and out of breath
10	n/a	**1.15**	159	1.80	146	Exhaustion

All RERs >1.1 are bold. When 95% predicted heartrate is reached, it is it is displayed in bold.
N/a=not applicable
*: Did not reach AT, **: AT could not be determined through Vslope method,

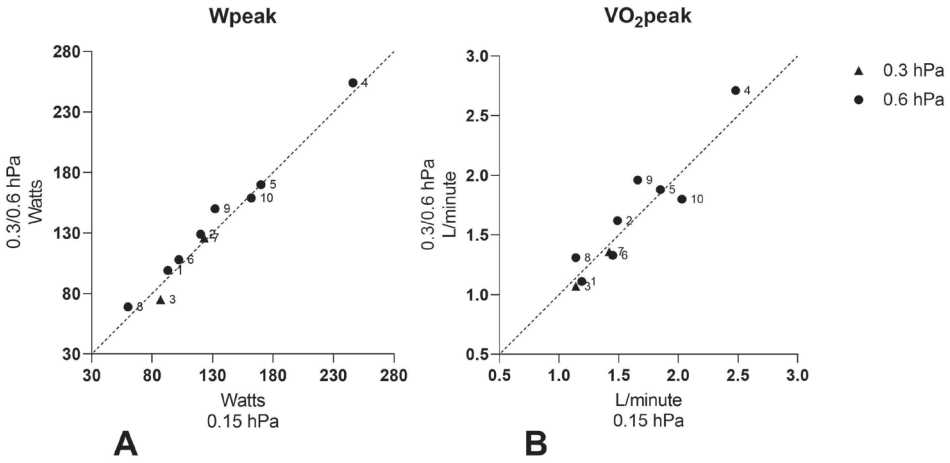

Figure 3. Intra-subject comparison for Wpeak and VO_2peak between the different HME resistances

A: Maximum workload. B: Peak oxygen consumption

Regular HME resistance (0.3 hPa [triangles] or 0.6 hPa [circles] compared to low resistance (0.15 hPa). The dashed line is the identity line.

	RER Lower resistance 0.15 hPa	Wpeak	VO_2 peak †	HR	Termination reason
	1.03	93	1.19	119	Coughing and dyspnea
	0.90	120	1.49	134	Exhaustion
	0.79	87	1.14	115	Unwell due emotional complaints of an unrelated life event
	1.26	246	2.48	167	Exhaustion
	1.16	170	1.85	127	Exhaustion
	1.03	102	1.45	133	Leg muscle cramps
	0.94	123	1.42	147	Leg fatigue and cramps, exhaustion
	0.95	60	1.14	127	Out of breath, exhaustion
	1.06	132	1.66	113	Dyspnea
	1.09	162	2.03	154	Exhaustion

†: the highest achieved measured VO2 in this test
Wpeak in Watts, VO_2 peak in L/min, 95% predicted HR is predicted heartrate calculated based on gender, age, weight and height.

Discussion

Cardiopulmonary exercise testing with gas exchange analysis is possible in laryngectomy patients wearing an HME. There was no air leakage during testing, all patients were comfortable wearing the connector during their CPETs, and there were no (serious) adverse events. However, less than half (4/10) of the patients reached an RER>1.1 in at least one test, and only one subject reached 95% of his predicted heart rate during one test. Thus, although this setup of CPET is technically feasible and appears to be safe, it could be questioned whether the used ramp protocol is suitable for reaching maximum exercise capacity in this population.

The subjects' reasons for terminating the CPET before reaching predicted maximum levels were mainly exhaustion, feeling out of breath, and leg fatigue, without signs of cardiopulmonary problems. Instead, early stopping was related to a low subjective exercise tolerance[30]. It is common that inactive patients do not tolerate normal acute physical responses induced by exercising. This can be trained and has proven to be effective in terms of properly performing CPET[31]. Although we purposefully sampled our participants based on regular physical activity of at least moderate intensity, most participants habitually participated in predominantly low-intensity activities such as cycling (some with electric assistance), moderate strength training, and walking. For selection of participants and determining the steps of the ramp protocol, we relied on self-reported levels of physical activity. However, in survivors of HNC, perceived levels of activity and fitness may not accurately reflect their actual levels[32]. This should be considered when determining the ramp steps in future testing.

Another explanation for patients stopping due to feelings of exhaustion and leg fatigue, could be that exercise capacity was limited by muscle strength, rather than aerobic capacity. Low skeletal muscle mass, sarcopenia, is relatively common (30-50%) in patients undergoing a laryngectomy[33,34]. Sarcopenia results in less muscle strength, affects gait, endurance and mobility, and may lead to inactivity which further impacts muscle mass and strength[35]. Limited muscle strength after laryngectomy could be a problem when using the current CPET protocols, which also calls for smaller increments.

Only one participant reached their maximum predicted heartrate once. Although this could be due to peripheral fatigue limiting the test, overestimation of maximum predicted heartrate is also common in low-fit subjects, and might be an alternative explanation for this finding[36,37].

Similar results to ours were found in a group of hemato-oncological patients during treatment: CPET (without breathing gas analysis) was found to be feasible and safe, but only a minority of patients reached maximal effort[28]. The researchers concluded that the protocol used might not be fitting for this low-fit and vulnerable group and suggested the use of an endurance protocol at fixed workload as a possible alternative. Although fixed-workload tests cannot be used to determine VO_2 peak, they can be useful to evaluate changes in exercise capacity over time in individuals, and for evaluation of intervention effects in comparative studies. The advantage of our current set-up is that it still enables breath-gas-analysis during such submaximal testing. As suggested by others, it would be an option to first train patients, before applying maximal CPET testing. For this purpose, muscle strength training, as well as aerobic training, have been suggested[28,38–40].

In the context of rehabilitation, the question remains whether reaching maximal capacity should be a testing goal, or whether individual testing goals should be set to match the patient's treatment goals, wishes and possibilities. Further research is warranted to determine the best approach to exercise testing in low-fit cancer survivors, including those after TL.

What stood out in the results of the patients reaching an RER>1.1 is the low relative peak VO2 (mean 19.3 ml/kg/min), especially considering their self-reported level of regular physical activity. As a reference: the minimum level of maximal oxygen uptake compatible with continued independence is about 15–18 ml/kg/min, normally reached at 80-85 years in sedentary elderly people[38].

In this sample, participants using the 0.3 hPa HME as regular HME had poorer exercise performance than participants using the 0.6 hPa HME. This is not likely the result of the HME used, but probably reflects that patients with a poorer general health or pulmonary condition choose a lower resistance HME for comfort.

In this sample, we found that lowering the HME resistance level did not lead to improved exercise capacity. Non-laryngectomized people tend to lower the breathing resistance during exercise by mouth breathing. So, we anticipated that a lower resistance would increase exercise capacity, but our data indicates otherwise. Of note; the resistance of the 0.6 hPa HME is still lower than that of nose breathing (1.9 - 3.9 hPa[41]). Those who are comfortable wearing a regular HME under non-exercise conditions likely will not benefit from a lower resistance HME during exercise. In addition, they must be aware that using low-resistance HMEs may feel more comfortable, but comes at the cost of reduced health benefits due to poorer performance of the HME in terms of heat and moisture retainment, and reduced training stimulus to the respiratory muscles.

Limitations

This is a small randomized and single-blinded exploratory study in which only self-reported active, predominantly male, laryngectomized patients have been included. Not blinding the researcher administering the test to the HME in use could have introduced performance bias. However, maximal encouragement was part of the standard operating procedure of the CPET. In addition, if a Pygmalion effect has occurred, this would likely have biased the findings towards better achievement using the lower resistance HME. Since we did not observe a difference, we deem such bias unlikely. The results should not be extrapolated to the larger population of laryngectomized patients. Since a comparison of the influence of regular HME resistance on exercise performance was beyond the scope of the study, there is no equal distribution of the two types of regular HMEs. As a pilot study, the study was not powered for statistical testing of differences. Hence, our findings and interpretation should be considered with caution. Lung function tests were not performed pre-CPET. In hindsight, this would have been useful to obtain a better assessment of pulmonary function as a potentially limiting factor.

Conclusion

This first exploratory study indicates that exercise-testing using breathing gas analysis with an HME in situ is safe and technically feasible to use in laryngectomized patients. The conventional ramp protocol may not be ideal for reaching maximum exercise capacity in this vulnerable group. We found no indications that lowering the HME resistance improves exercise capacity in this study.

Appendix B: Explanation of subparts of the CPET

TT = Time in Test, in seconds
Maximum Workload (Wpeak)= maximum workload achieved during CPET in Watts
Heartrate= heartbeats per minute
VO_2**peak =** maximal oxygen consumption in L/minute during testing
Relative VO_2 **=** maximal oxygen consumption corrected for weight, in mL/kg/min
VE peak = Maximum ventilation in L/minute
RER= respiratory exchange ratio is the ratio between the metabolic production of carbon dioxide (CO_2) and the uptake of oxygen (O_2)
Anaerobic threshold= Moment when the oxygen consumption rises above a point in which aerobic energy production is supplemented by anaerobic mechanisms, causing a sustained increase in lactate and metabolic acidosis, in VO_2/kg
VE/VCO_2 **at anaerobic threshold =** Minute ventilation/carbon dioxide production at the moment of anaerobic threshold
Perceived level of exertion= Borg-score[24]; a 15-point scale (6 to 20) used to rate subjective experiences during physical exertion. Score ranges from 6 (no effort) to 20 (absolute maximum effort)
95% predicted heartrate = 95% of the maximum predicted heartrate based on age, formula: (211 - 0.64*age)*95%, heartbeats per minute

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Chapter 10

Singing after Total Laryngectomy

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European Annals of Otorhinolaryngology, Head and Neck Diseases, September 2023

Dear Editor-in-Chief,

As recently pointed, in the *European Annals of Otorhinolaryngology Head & Neck Diseases*, 2023 is the 150th anniversary of the description of the total laryngectomy technique by Theodor Billroth[1-3]. We know, singing is not the first thing to think about after a total laryngectomy. This invasive surgery has life-changing consequences; patients must learn to speak, swallow and smell again. They often face psychological and social distress, decreased quality of life, and decreased respiratory function, might suffer from a hypo- or hypertonic voice and face less intelligible speech. With this letter, we would like to pay attention to the possibility and benefits of singing on respiratory function, voice quality, and quality of life.

In our institute, the 56-year-old writer Willem Melchior, who is nowadays nine years disease-free, was diagnosed in 2012 with T2N0M0 glottic squamous cell carcinoma and treated with radiation therapy. In 2013, a local recurrence was noted, and a partial laryngectomy with the CO2 laser performed. In 2014, total laryngectomy became unavoidable and was performed. The surgeons performed a primary puncture and placed a Provox Vega® voice prosthesis during that same surgery. Our patient started voice rehabilitation on the 12th day post-surgery and could directly speak using tracheo-esophageal speech. After a couple of weeks, he wished to learn to speak without hands. After a few practice sessions, he was successful in handling and speaking with the Provox FreeHands HME®. Pre-surgery, one of his hobbies was singing and playing guitar. After his laryngectomy, he started singing again, created a Youtube Channel, and uploaded videos of himself singing Dutch songs and French chansons. He found that singing brings him joy. He pays attention to clear articulation, phrasing, and pausing during singing. Besides fun, he also has challenges to cope with. For instance, he has to choose songs that are not too fluctuating in tone. Also, he has to control the (air) pressure build-up because too high pressures loosen his adhesive with the consequences of air leakage. The FreeHands HME® allows him to play the acoustic guitar simultaneously, although he has to play it softly; otherwise, his voice is not audible.

Singing after a total laryngectomy is not new. In 2013, Onofre et al.[4] investigated singing as a 12-session therapy method and found that roughness, breathiness, and vocal extension all improved. All participants presented tuning, and almost all showed a more significant presence of legato[4]. Continuing in time, specific choirs for laryngectomees has been set up. For instance, we are aware of the total laryngectomized choral that Professor Louis Traissac from the Bordeaux University set up in France before he retired. In 2016, Dr. Thomas Moors started the charity (and choir) Shout at Cancer. This charity implements singing and acting techniques in voice rehabilitation after a

total laryngectomy. Dr. Moors, who wrote an article on www.entandaudiologynews.com, found improved volume, pitch range, phrase length and voice control in the participating patients after six sessions of singing. He stated that, beside all the functional favors of singing, it also promotes the acceptance of their new voice and might even boost the self-confidence of laryngectomees. The preliminary evidence of Fancourt et al.[5] endorses the psychological favors. They concluded that singing might improve mood state and reduce stress in cancer patients[5]. With all the physiological and psychological benefits in mind, please enjoy the beautiful songs of our laryngectomee and dare your laryngectomized patients to start singing (https://www.youtube.com/channel/UCM7JxVaNp52J8tCt3cCguQg).

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Agreement

Willem Melchior signed the agreement to participate in this letter and wanted to be mentioned by his full name.

Chapter 11

General Discussion and Future Perspectives

General Discussion and Future Perspectives

This thesis focuses on improving head-and-neck cancer (HNC) care by exploring two aspects: shared decision-making (SDM) and rehabilitation strategies.

The first part of the thesis aimed to provide insights into the prevalence of decisional conflict and decision regret among HNC patients, and secondly, to explore the development and impact of patient decision aids (PDA) (Part 1: Shared decision-making). The aim for the second part of this thesis was to evaluate and enhance tools, designed specifically for individuals following total laryngectomy (TL), aiming to assess and refine newly developed products for improved patient outcomes (Part 2: rehabilitation after TL).

Summary of the findings

Part 1: Shared Decision-Making in Head and Neck Oncology

In **Chapter 2** we saw that, although limited data on Decisional Conflict (DC) and Decision Regret (DR) were available, the performed studies indicated that DC and DR are highly prevalent issues in HNC. Results suggest that study-specific questionnaires underestimated DR. The findings underscore the rationale to improve counseling and shared decision-making for this specific patient population. **Chapter 3** showed that the observed level of shared-decision making (SDM) in our tertiary oncologic center was scored as moderate, yet both patients and surgeons perceived SDM more positively than observed in the scoring. Surgeons particularly do well discussing treatment options and forming partnerships, but surgeons often wrongly assume patients' preference for involvement.

In **Chapter 4**, we found that almost all patients with advanced laryngeal carcinoma experience high levels of DC, and that the level of knowledge regarding treatment options was low, indicating for better patient counseling. In **Chapter 5** showed that the patient decision aid for patients with advanced laryngeal cancer effectively reduced decisional conflict, enhanced patients' knowledge and improved perceived SDM.

The last chapter of this section, **Chapter 6**, displays the development of a PDA for early stage oropharyngeal cancer patients considering surgery or radiotherapy, as treatment options. The decision aid emphasizes the disparities in short- and long-term side effects between the two treatments. Patients and physicians found the decision aid to be understandable, user-friendly, and helpful for future patients.

Part 2: Rehabilitation after TL

In **Chapter 7**, we showed that prophylactic replacement of voice prostheses after TL is not feasible due to high inter-and intrapatient variation in device lifetime. We tested a new voice prosthesis (PVHP) in laryngectomized patients in **Chapter 8**, and found that acceptance of the PVHP is largely dependent on device lifetime, decreasing from 87% to 40% after leakage or replacement. Voice quality remains consistent across different VPs.

In **Chapter 9**, we found that Maximal Cardiopulmonary Exercise testing in laryngectomized patients is feasible, however the protocol does not seem appropriate to reach this group's maximal exercise capacity. Lowering HME resistance does not increase exercise capacity in this cohort.

Lastly, in **Chapter 10**, we describe one of our laryngectomized patient's ability to sing with a hands-free voice prosthesis, allowing him to simultaneously play guitar.

Part 1: Shared Decision Making in Head and Neck Oncology

Head and neck cancer (HNC) often needs drastic and complex treatments, affecting patients' quality of life. Complex treatment choices, like balancing survival and organ preservation or equally effective options, are preference-sensitive, putting patients at risk of decision conflict (DC)[1,2]. DC is the uncertainty experienced when making a difficult decision due to feeling uninformed or conflicted about outcomes, and has many negative consequences, such as delay in decision-making, making treatment choices that are not in line with patients' preferences, and decisional regret[3,4]. Decisional regret (DR) is a negative feeling associated with grief, disappointment, or distress following a decision regarding healthcare. Our systematic review regarding the prevalence of DC and DR in HNC patients (**Chapter 2)** showed that there is limited research performed regarding this topic, only 28 studies were performed between 1987 and 2022, with more studies later in years. In most studies, DC and DR were secondary outcomes and studies were quite heterogeneous on multiple fronts. The fact that most studies used it as secondary outcomes shows that clinicians and researchers have prioritized other primary outcomes. Especially results on DC were lacking, making it hard to draw conclusions, although we did see that 25-50% of the HNC patients did experience DC and qualitative research showed that stress of diagnosis and lack of clear information regarding disease, treatments, and their impact, led to a high level of DC in most patients. We investigated DC in patients with advanced laryngeal cancer (**Chapter 4)** and found that nearly all patient experienced clinically significant levels of DC. We examined the effect of a PDA on DC among these patients (**Chapter 5)**. The PDA improved knowledge levels and perceived SDM, leading to a significant reduction in overall decisional conflict scores, indicative of improved decision-making. Despite these gains, the proportion of patients experiencing clinically significant DC remained high and was similar across groups, highlighting the complexities involved in decision-making for this patient population. We found higher levels of DC, than we found in our SR. This may be attributed to the specific stage and type of HNC, as well as the fact that this study focused on this primary outcome and was specifically powered for it. In contrast, other studies treated it as a secondary outcome and often included mixed groups of tumor types and stages. Additionally, cultural factors and timing could also play a role[5,6]. When looking at other tumor types, our found prevalence of CSDC is much higher compared to for example breast cancer (16-68%[7,8]) and prostate cancer (46-63[9,10]). Although also in these studies data is hard to compare due to heterogeneity in tumor stage and treatment possibilities. It is assumable that tumor stage influences the level of DC, although we do not have research to prove this. But looking at those numbers, we can also state that HNC definitely has higher scores compared to other tumor types, and way higher than in primary care (10-31%[11]). How can we explain this? One could hypothesize that this is due to the critical functions affected, like speech and

swallowing, making treatment decisions complex. The aggressive nature of these cancers often necessitates combined treatments like surgery, chemotherapy, and radiation, which come with significant side effects. Understanding these treatment options can be challenging for patients, as the complexities of treatment and the high impact of side effects often lead to uncertainty. This is further compounded by socioeconomic barriers and health literacy limitations. Visible disfigurement and the psychosocial impact also add to the difficulty of decision-making, making it more challenging for this group compared to those with other cancers. However, there is a lack of research to support this.

DR has been more extensively studied in our field (**Chapter 2**). The results are heterogeneous, and study-specific questionnaires underestimate the prevalence of DR (5-35%) compared to validated questionnaires (SSS 72-86%, DRS 14-86%). Factors like tumor location, stage, treatments, timing, and complications influence DR, but the studies did not allow clear comparisons among patient groups. Therefore, caution is needed when interpreting DR prevalence. The risk of depression is significant in HNC and you could hypothesize that it might be linked to DR[12]. The emotional burden of diagnosis, disfigurement, and functional impairments due to treatment can exacerbate DR. Overall, DC and DR are highly prevalent in HNC patients and warrant attention in clinical work and research.

A more precise understanding of the prevalence and nuances of DC and DR in HNC patients could significantly influence counseling practices, potentially promoting SDM approaches. We observed a moderate level of SDM within our center (**Chapter 3)**. However, our analysis revealed a notable discrepancy between perceived and observed SDM scores. This discrepancy suggests that both patients and surgeons may lack a comprehensive understanding of what SDM truly involves. Interestingly, both groups tended to perceive a higher level than what was objectively observed.

Comparisons with similar research in other fields indicate that our observed SDM scores were relatively high (low levels in breastcancer[13], low-moderate in hepatobiliary surgical[14] and similar in vascular surgery[15] and anesthesiology[16]). This could be due to the complexity of HNC and its significant treatment implications, which may inherently prioritize patient-centered interactions.

However, there are some methodological considerations regarding these results. The SDM-Q-9 questionnaires used may not adequately capture perceived SDM, given the paradoxical results found between objective and perceived scores. If patients are unaware of what to expect, they might rate their physicians highly even when observed levels are lower. Another question that arose was: If patients rate their perceived SDM this high, do we need improvement?

SDM has been proven to reduce DC and DR, while increasing patient satisfaction. Therefore, further enhancements in SDM practices could potentially provide significant benefits to patients. Furthermore, robust SDM practices help align treatment decisions with patients' values, goals, and preferences. This alignment ultimately leads to better adherence to treatment plans and improved health outcomes[17–19]. Even though patients believe they are receiving sufficient SDM, the discrepancy between their perception and observed levels indicates gaps in understanding and engagement. Improving SDM practices will ensure patients have a clearer understanding of their options, empowering them to make informed decisions that align with their values. Therefore, enhancing SDM should remain a priority to ensure patients are well-informed, engaged, and supported in making decisions that best suit their needs. To enhance counseling practices and foster a more robust implementation of SDM, further education and training are needed for both patients and healthcare providers.

However, a critical barrier to widespread SDM adoption lies in the prevailing apprehension among some physicians. Concerns regarding patient decision-making capabilities and the fear of patients choosing options deemed unfavorable by clinicians underscore a fundamental mindset shift that must occur within the medical community. Educating and empowering healthcare providers to embrace SDM as a collaborative process, grounded in respect for patient autonomy and informed choice, will be essential in fostering a culture conducive to its widespread integration. Throughout the years this has improved due to the integration of SDM training into the Dutch medical curriculum, enhancing the foundational knowledge among healthcare professionals. Additionally, public awareness campaigns like 'Samen Beslissen' ('Shared Decision-Making')[20] have increased the visibility and perceived importance of SDM. It has also been adopted into the healthcare visions of the Federation of Medical Specialists in the Netherlands[21], signaling a formal recognition of its value. Moreover, ongoing research has expanded understanding and developed effective SDM tools, further supporting its practical application in clinical settings. This comprehensive approach has gradually transformed how decisions are made in healthcare, emphasizing collaboration and patient involvement.

An SDM tool that is very popular at this moment is the patient decision aid (PDA). PDAs are tools designed to help patients understand their medical options, benefits, and risks, aiding them in making informed healthcare decisions that align with their personal values. They serve to bridge the information gap between patients and clinicians, promoting a more collaborative decision-making environment. PDAs are now being actively developed across various medical fields. Some commercial companies specialize in designing and implementing these tools in collaboration with different

departments. Their emergence is strategic, given that creating a decision aid is a time-consuming and complex task due to its multidisciplinary nature. Additionally, there are associated costs, such as web hosting, creating videos and animations, and ensuring regular maintenance and updates. Quality assurance for PDAs is maintained through adherence to the International Patient Decision Aid Standards (IPDAS) criteria[22]. These guidelines ensure that PDAs are evidence-based, accurate, and unbiased, promoting clarity and consistency while helping patients make well-informed decisions.

We've developed a PDA for patients with early-stage oropharyngeal squamous cell carcinoma (OPSCC), providing them with valuable guidance in navigating treatment decisions between radiation therapy and transoral (robotic) surgery (**Chapter 6**). Despite incorporating numerous images and explanatory videos, challenges remain for those without computer access or literacy skills, highlighting the need for more inclusive tools that can accommodate diverse patient needs. The impact of the PDA for advanced laryngeal cancer showed that knowledge increased significantly, as that the level of DC.

Despite promising outcomes, integrating PDAs into routine clinical practice poses challenges, necessitating concerted efforts to address logistical barriers, healthcare provider attitudes, and institutional policies. Ultimately, fostering a culture that prioritizes patient involvement in decision-making is essential to ensure that PDAs fulfill their potential in supporting informed decision-making and enhancing patient outcomes. Potential solutions include assigning specific individuals to oversee the process, discussing PDAs during multidisciplinary team meetings, and incorporating them into patient portals or environments. Recognizing that tasks requiring time and effort can easily be overlooked or deprioritized, it's crucial to make the implementation as straightforward as possible.

Part 2: Rehabilitation after Total Laryngectomy

After a TL, vocal rehabilitation is needed. In most Western countries, the use of a voice prosthesis is (VP) the gold standard[23]. VPs have been available since the 1980s and have been developed by Dr. Mark Singer and Dr. Eric Blom[24]. Modern prostheses, typically made of silicone, are essential tools for vocal rehabilitation post-laryngectomy. However, their limited lifespan remains a significant issue for patients. These devices require periodic replacement due to factors such as leakage, bacterial colonization, or mechanical wear[25,26]. The need for regular replacements can be burdensome for patients, as it requires frequent, unplanned, medical visits and procedures. Additionally, these replacements can be costly (if not reimbursed) and may lead to interruptions in speech. Variability in prosthesis lifespan across studies reflects differences in patient anatomy, lifestyle, and maintenance, which further complicates their management. This makes long-term rehabilitation challenging, highlighting the need for more durable, user-friendly prostheses.

Chapter 7 highlights the challenges associated with prophylactic replacement of voice prostheses (VPs) in laryngectomized patients, revealing that such an approach is not feasible due to the high variability in device lifetime. While prophylactic replacement has been successful in other medical devices like pacemakers, the unpredictable nature of VP device lifetimes makes it impractical for routine application[27]. Despite the potential benefits of planned replacements in reducing unexpected VP leakages and improving patient quality of life, the study's findings suggest that such a strategy would lead to increased clinic visits without clear benefits in preventing complications and a high frequency of needed visits. The results were so clearly unhelpful that, given the current VPs, further prospective investigation seems not to be recommended. Fortunately, new VPs are developed, as we investigated the Provox High Performance (PVHP), which was intended to be a more affordable VP (than the ActiValve) with a predictable and prolonged device lifetime (**Chapter 8**). The PVHP is made of silicon rubber with a fluoroplastic valve flap and valve seat, a material that resists biofilm destruction similar as in ActiValve[28], but without the use of a valve magnet. Fluoroplastic is a sticky material, for which the use of a lubricant is needed to prevent blockage of speech[29,30].

While initial acceptance of the PVHP was relatively high, dropping to 40% after device replacement due to failures, key issues such as valve stickiness affecting speech were reported. Interestingly, despite objective assessments indicating no significant improvement in voice quality with the PVHP, half of the patients subjectively rated their voice quality and speaking effort better compared to their regular VP. This discrepancy

suggests a potential influence of cognitive biases like the “new is better” heuristic. The study underscores the necessity for further research and development to tackle the multifactorial challenges affecting voice prosthesis longevity. Large patient cohorts are crucial for in vivo evaluations and finding voice prostheses (VPs) with improved lifespan remains essential for enhancing patient quality of life. One valuable direction could involve focusing on patients who underwent total laryngectomy (TL) without (chemo)radiation, so you have the most homogenous sample. The challenge lies in finding VPs suitable for all patients. While fluoroplastics may offer strong resistance to bacterial colonization, their rigidity could lead to early device issues. Titanium, although promising, is quite rigid, but 3D printing could allow customized designs that match a patient’s specific stoma size. However, this approach would not be feasible in the initial months following TL due to stoma healing. An alternative could involve silicone VPs enhanced with hydrogels or coatings to reduce biofilm formation, maintaining flexibility while offering better bacterial resistance. Further research is necessary to address the remaining challenges and fully understand the multifaceted issues involved.

Heat and moisture exchangers (HMEs) play a crucial role in managing the respiratory health of patients. With the removal of the larynx, the natural humidification and warming of the air are lost, often leading to significant pulmonary challenges like excessive mucus production, coughing, and crusting around the stoma. HMEs function as artificial noses, capturing the warmth and humidity from exhaled air and returning it to the inhaled air. This reduces pulmonary complications by maintaining moisture in the airway and improving mucus viscosity[31]. However, some patients find that the airflow resistance through certain HMEs can be too high, making breathing through the stoma difficult or uncomfortable. Selecting the appropriate HME with optimal resistance is essential for balancing effective moisture retention with patient comfort. Regular use of well-matched HMEs helps minimize stoma blockages, reduce coughing, and improve overall quality of life by ensuring that patients can breathe more comfortably and manage their airways better[31].

We have looked at the influence of the resistance of HMEs during Cardiopulmonary exercise testing (CPET) with gas exchange analysis (**Chapter 9**). We have also shown that CPET is technically feasible and safe for laryngectomy patients using HME. However, the study raises questions about the suitability of the ramp protocol used in reaching maximum exercise capacity in this population, as less than half of the participants achieved the predicted maximum levels. Reasons for early termination of CPET included exhaustion, breathlessness, and leg fatigue, suggesting that perceived exercise tolerance might be a limiting factor. Moreover, limitations in muscle strength,

possibly due to sarcopenia, could also affect exercise capacity, highlighting the need for tailored CPET protocols for laryngectomy patients.

The current protocol may not be suitable for using CPET as a baseline for exercise rehabilitation, especially for patients who underwent laryngectomy a significant time ago. Conducting spirometry prior to a CPET could improve gas analysis interpretation, particularly since many laryngectomy patients are (former) smokers and may have COPD, which could influence test outcomes. A submaximal exercise test, such as the six-minute walk test, would be more appropriate. If this test shows that a patient can tolerate maximum exertion, then a CPET could be feasible. However, I would advocate for a progressive exercise plan based on the six-minute walk test, as walking is beneficial for nearly everyone, making it a practical and achievable activity that could lead to more realistic rehabilitation goals and meaningful results.

Chapter 10 beholds a letter to the editor. This letter underscores the unique case of a former patient, whose journey of resuming singing after total laryngectomy sheds light on the therapeutic potential of music for patients undergoing similar procedures. By sharing his story and the challenges he faces, such as managing air pressure and song selection, the letter emphasizes the importance of exploring creative avenues for rehabilitation beyond traditional methods. Furthermore, it references existing research and initiatives, including choirs for laryngectomees and therapeutic singing programs, which suggest that singing can offer not only physical benefits but also psychological ones, such as improved mood and self-confidence. Encouraging laryngectomy patients to embrace singing as part of their recovery journey not only promotes holistic healing but also empowers them to explore their full potential beyond the confines of their medical condition. Healthcare professionals can play an active role in this by setting up these programs. This is a very proactive patient, but how do we engage those who are less extroverted? This is a crucial aspect of rehabilitation. Besides singing, other activities might also be beneficial, such as swimming with a 'Larkel'[32]. Engaging in hobbies or activities that make individuals feel valuable again can be a potent component of rehabilitation. This approach not only helps patients recover physically but also rebuilds their sense of self-worth and community involvement.

Future perspectives

Having thoroughly discussed all our research, the question arises: What is next, and above all, what do I think the future will look like?

Part 1: Shared decision making

One of the studies that is still ongoing is the one investigating the impact of our developed PDA for early stage oropharyngeal cancer patients. With collaborative efforts from other institutions, our aim is to conclude this investigation by approximately 2027. Additionally, there is a pressing need for an updated iteration of the advanced laryngeal cancer PDA. This entails a thorough review to ensure compliance with the latest clinical guidelines, alongside streamlining the content for enhanced clarity and accessibility.

Furthermore, leveraging the rich data from our patient interviews documented in Chapter 3, we are embarking on qualitative research pertaining to nudging techniques and aligning patient goals during counseling sessions. Our ultimate objective is to convene a comprehensive meeting involving all participating physicians, where we can collectively scrutinize the findings and potentially provide tailored training in SDM.

What I've noticed is that navigating the landscape of SDM implementation presents significant challenges, especially in multicenter settings. While multicenter studies are crucial due to the relatively low numbers of HNC patients, rallying participation from diverse institutions proves to be a formidable task. Overcoming logistical hurdles and fostering collaboration among stakeholders will be paramount in realizing the full potential of SDM initiatives. In the Netherlands, we do have a dedicated working group for head and neck tumors, and there is a great deal of collaboration. However, submitting a study in another hospital and achieving patient inclusions remains difficult. To improve collaboration, establishing clear communication protocols and regular cross-institutional meetings could help align goals and methodologies. Additionally, leveraging digital tools for data sharing and project management can streamline processes and enhance transparency among all participating centers.

In envisioning the future landscape of healthcare, my hopes are pinned on a fundamental shift in the mindset of physicians. It's imperative that we recognize patients as individuals with unique preferences and needs, steering away from a one-size-fits-all approach to treatment. As echoed in the words of Hippocrates, "Our primary aim should be to treat the patient, not just the disease". This paradigm shift towards

patient-centered care is not merely a lofty ideal but a practical necessity. By aligning treatment plans with patients' desires and values, we can anticipate a shift towards less invasive interventions and a prioritization of quality over mere quantity of life.

While this thesis primarily delves into specific aspects of SDM, it's crucial to acknowledge that there are myriad pathways to achieve patient-centered care. Embracing a holistic approach to medicine entails recognizing and valuing the diverse avenues through which patients can actively participate in their healthcare journey. In this vein, I wholeheartedly recommend Atul Gawande's insightful book, "Being Mortal: Medicine and What Matters in the End[33]," as essential reading for every physician (and I would definitely recommend his other books as well). Through poignant narratives and thought-provoking insights, Gawande navigates the complex terrain of end-of-life care, offering invaluable perspectives on the essence of patient-centered medicine. Initially, Gawande himself did not practice SDM, but he shares his own story about how he became more passionate about this approach, underscoring the transformative impact it can have on both patients and healthcare providers. This makes me believe that adopting SDM is possible, but it will certainly take time for physicians who have been practicing for a longer period to make this transition.

Looking ahead, the horizon appears promising for the integration of SDM and patient-centered care into the fabric of Dutch healthcare. Notably, SDM has been integrated into the Dutch medical curriculum, marking a significant step towards prioritizing patient empowerment and involvement in healthcare decisions. Furthermore, the advent of artificial intelligence (AI) holds promise in augmenting these efforts, potentially serving as a valuable tool in facilitating SDM processes[34,35].

I hope to see all SDM tools integrated into patient records, with AI potentially reminding physicians during consultations to inform patients about these tools. Alternatively, AI could automatically identify the correct patients and send them the PDAs and information. However, please keep in mind that this should complement, not replace, the physician consultation. These patients are vulnerable, and while many tasks can be automated, they also need the opportunity to discuss their emotions, fears, and concerns with a real person. This personal connection is essential, as they will be seeing their oncologist for at least five years.

Part 2: Rehabilitation after total laryngectomy

For rehabilitation after TL, there are numerous possibilities for improvement, but each comes with its own challenges, such as costs. Additionally, investigating all these interventions is difficult due to the low number of patients.

Considering the complexity of the challenges associated with VPs and HMEs, it's imperative to explore innovative approaches for enhancing their performance and longevity. One avenue worth exploring is the development of advanced tracking mechanisms to monitor the lifespan of VPs. Simplifying the issue, we could envisage a solution where a specialized layer on the surface of the voice prosthesis undergoes a color change as bacterial and fungal growth accumulates. This visual cue could prompt patients to schedule a replacement appointment once the designated color threshold is reached. However, implementing such a solution poses considerable hurdles. Questions abound regarding the nature and sensitivity of this color-changing layer, its compatibility with diverse throat flora compositions, and the associated costs. While the concept is appealing in theory, practical implementation presents significant challenges. Patients must navigate the intricacies of detecting subtle color changes amidst mucus and crusts, thereby complicating the reliability of this method. Moreover, ensuring universal applicability across varying patient demographics further compounds the feasibility of this approach. Thus, while innovative, this concept may not offer a viable solution in its current form.

But allow us to just think out loud. Does a VP need to be located in a patient's throat? Wouldn't it be possible to redesign the whole concept, and develop something that does not have to be located in such a vulnerable place? Perhaps a completely new approach to laryngectomy. Yes, the tumor needs to be removed and the airway needs to exit somewhere, but can't we rethink the location and even the objective of the voice prosthesis itself? Or, can we create a new larynx for a patient? Consider the possibilities with 3D printing. I know it sounds far-fetched at this moment (and it is), but the internet was only just invented in 1969, and look where we are now! Or growing new limbs? There are, of course, many ethical considerations surrounding this, and I'm not sure if I'm for or against it, but the idea is quite interesting, right? Sea stars and some lizards can regrow limbs—could we try this for humans?

As we redesign the whole concept of TL, hopefully HMEs won't be necessary for patients either. But until then, maybe some easier solutions would help. There is already a reusable metal 3D-printed HME[36]. If we can design HMEs that fit patients' airway resistance and make them adjustable for use during exercise, this would greatly benefit patients' quality of life and, of course, adherence, and leading to fewer pulmonary complaints. As for CPET, at this moment, I think this is a bridge too far for many patients. We could definitely benefit from research that delves into the exercise responses of laryngectomized patients. This would make it possible to develop tailored exercise programs, especially since we have shown that exercise testing with gas exchange analysis is feasible using our 3D-printed adapter.

As our medical capabilities continue to expand, it's imperative to engage in ongoing dialogue with patients, asking essential questions about how treatment options might impact their lives. Rather than solely considering technical feasibility, we must prioritize understanding whether a proposed intervention aligns with a patient's goals and aspirations, ultimately striving to enhance their overall well-being. We need motivated and trained healthcare workers, but patients also need to be educated on what they can expect from their physicians. Choosing a treatment is teamwork, and I am committed to being part of that team.

Returning to the story of Mr. T, he experiences decisional regret, which significantly impacts his quality of life. He is struggling with the limited lifespan of his voice prosthesis and has stoma issues that require surgical adjustments.

My goal is to minimize patient dissatisfaction with their chosen treatment. I hope that this dissertation represents a small step in that direction, but the journey doesn't end here. Understanding that every person is unique and striving to treat each patient as if they were a member of your own family is a guiding principle I aim to pursue throughout my medical and scientific career.

For Mr. T, it's too late, but hopefully, we can prevent others from experiencing similar challenges in the future.

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Chapter 12

Summary & Samenvatting

12.1 English summary

This dissertation consists of two parts, focusing on different aspects of care for head and neck cancer (HNC). The first part addresses shared decision-making (SDM), particularly in advanced laryngeal cancer and early stage oropharyngeal cancer where primary curative surgery and radiation are both options. The second part focuses on various tools used in the rehabilitation of patients after a total laryngectomy (TL), aiming to improve outcomes for TL patients.

Chapter 1 is a general introduction that provides background on head and neck cancer, specifically laryngeal and oropharyngeal cancer. It discusses the complexity of decision-making, the importance of a multidisciplinary approach, and the impact of the disease on patients' lives. The need for shared decision-making (SDM) and the role of patient decision aids (PDAs) are emphasized to support patients in their treatment choices. The second part highlights the necessity of specialized rehabilitation after a total laryngectomy, focusing on voice prostheses (VP) and Heat and Moisture Exchangers (HME). VPs enable patients to learn to speak again, although their limited lifespan leads to unplanned hospital visits for VP replacement. HMEs warm and humidify the airway, reducing pulmonary complaints, but their fixed resistance can cause breathing difficulties during intensive activities, leading to limited use.

Part 1: Shared Decision Making in Head and Neck Cancer

Chapter 2 is a systematic review with meta-analysis that examines the current literature on the prevalence of decisional conflict (DC) and decisional regret (DR) in HNC patients. The findings indicate that DC and DR are significant issues for a large percentage of patients. Despite the limited number of studies and variability in patient groups, tumor locations, stages, and questionnaires used, it is clear that DC and DR are prevalent among HNC patients. These findings highlight the urgent need for improved counseling strategies and decision aids to support patients in making informed treatment choices. The review underscores the importance of addressing these psychological factors to enhance patient outcomes and satisfaction with their treatment decisions.

In **Chapter 3**, the current state of observed and perceived SDM among head and neck surgeons, patients, and their relatives within our own institution was investigated. We measured perceived levels of SDM and patient involvement using questionnaires and analyzed observed SDM by studying audiotaped consultations. Our results showed that surgeons and patients overestimate the extent of SDM compared to actual observations. Despite high perceived SDM scores, observed scores were moderate.

There was a positive association between the duration of consultations and observed SDM scores. Our findings suggest that more attention should be paid to patients' goals, values, and preferences during consultations to improve SDM quality.

Chapter 4 examined knowledge levels, decisional conflict and perceived SDM in patients with advanced laryngeal cancer who could choose between larynx-preserving treatment or a total laryngectomy, both options having significant impact on their quality of life and differ in survival rates. The study revealed that nearly all participants (98%) experienced significant decisional conflict after counseling. Additionally, patients' knowledge of treatment options was low, with an average correct response rate of 47% on knowledge questions. This lack of understanding, especially regarding laryngectomy, underscores the need for improved patient education, despite reasonably high levels of perceived SDM reported by both patients and physicians.

Chapter 5 follows up on Chapter 4 by investigating the impact of a newly developed PDA on these patients. The group using the PDA showed less decisional conflict and greater knowledge compared to the standard procedure group (Chapter 4). They also experienced higher levels of perceived SDM. The results indicate that using a PDA contributes to more effective decision-making for patients with advanced laryngeal cancer by reducing decisional conflict and enhancing knowledge and perceived SDM.

Chapter 6 describes the development of a PDA for patients with oropharyngeal cancer eligible for curative surgery or radiation therapy. Using international standards and methods such as in-depth interviews and think-aloud sessions, this decision aid was designed to clearly explain treatment options. It was extensively evaluated and adjusted with input from both survivors and medical specialists, resulting in a user-friendly and informative tool. The decision aid highlights differences in short- and long-term effects between surgery and radiation and is appreciated for its clarity and usefulness in the decision-making process.

Part 2: Rehabilitation after Total Laryngectomy

In **Chapter 7**, we investigated whether the prophylactic replacement of VPs could prevent leaks in patients after TL. These leaks negatively impact patients' quality of life and lead to unplanned hospital visits. We analyzed data from patients treated between 2000 and 2012 at the Netherlands Cancer Institute. Our results showed significant variability in VP lifespans both between and within patients, making prophylactic replacement impractical. Predicting VP lifespan and setting

a preventive replacement schedule is challenging. Mathematical simulations indicated that preventing 70% of leaks through prophylactic replacement is not feasible, suggesting this strategy is not viable due to the high variability in VP lifespans.

Chapter 8 tests the new Provox Vega High Performance (PVHP) voice prosthesis, designed for longer and more predictable lifespans. We assessed patient acceptance, adverse events, voice quality, and device lifespan. Patients who previously used a Provox Vega or ActiValve Light were evaluated over two weeks. Of the fifteen participants, 87% accepted the PVHP after two weeks, but this dropped to 40% after leakage. The median lifespan of the prostheses was 64 days. Voice quality did not differ between the PVHP and standard prostheses. The most reported adverse event was valve stickiness (46%). Acceptance of a new VP strongly depends on its lifespan, which remains a challenge.

In **Chapter 9**, the feasibility of maximal cardiopulmonary exercise testing (CPET) in patients after laryngectomy with an HME in situ was assessed, using a specially designed connector. We also examined the effect of different HME resistances on exercise capacity in this group. Ten participants underwent two CPETs with their daily HME (with different resistance levels) and one specifically developed for activity (very low resistance), with the order randomized and blinded. All participants completed both tests without adverse events. Only four participants reached a Respiratory Exchange Ratio (RER) >1.1 in at least one test. Maximum exercise levels did not differ with HMEs of varying resistance. Although CPET with an HME is feasible, the protocol does not seem suitable to reach the group's maximal exercise capacity, and lowering HME resistance does not increase exercise capacity in this cohort.

Chapter 10 shares the inspiring story of a laryngectomy patient who, despite the major surgery, relearned to sing and play guitar. After his total laryngectomy, the patient began voice rehabilitation and quickly mastered tracheoesophageal speech and hands-free speaking. His passion for singing led to the creation of a YouTube channel where he shares videos of himself singing Dutch songs and French chansons. This story demonstrates that singing after a total laryngectomy can improve respiratory function and voice quality, enhancing patients' quality of life and self-confidence. It highlights the value of music and singing as rehabilitation tools and sources of joy.

In **Chapter 11**, all the aforementioned chapters are discussed and contextualized. The dissertation aims to improve head and neck cancer care by exploring shared decision-making (SDM) and various aspects of rehabilitation after TL.

Looking to the future, Chapter 11 underscores the need for further development and refinement of SDM practices. There is a lack of research in this field, despite the fact that these patients undergo significant and life-changing treatments, and SDM can offer them substantial benefits. For rehabilitation tools, future research should focus on improving the durability and user-friendliness of voice prostheses. Technological innovations, such as artificial intelligence, may play a role in enhancing SDM and personalizing rehabilitation programs. These steps can support future patients in their journeys and potentially improve their quality of life.

12.2 Nederlandse samenvatting

Dit proefschrift bestaat uit twee delen, gericht op verschillende aspecten van zorg bij hoofd-halskanker (HNC). Het eerste deel behandelt gedeelde besluitvorming, met name bij gevorderde larynxkanker (strottenhoofd), en orofarynxkanker (mond-keelholte) waarbij genezende chirurgie een behandeloptie is. Het tweede deel richt zich op verschillende hulpmiddelen die gebruikt worden bij de revalidatie voor patiënten na een totale laryngectomie (TL, het verwijderen van het strottenhoofd), met als doel de uitkomsten voor TL-patiënten te verbeteren.

Hoofdstuk 1 is een algemene introductie die achtergrond geeft over hoofdhalskanker en specifiek larynx- en orofarynx kanker. Er wordt ingegaan op de complexiteit van de besluitvorming, het belang van een multidisciplinaire aanpak en de impact van de ziekte op het leven van de patiënten. De noodzaak van gedeelde besluitvorming (shared decision making; SDM) en de rol van keuzehulpmiddelen (patient desicion aids; PDA) worden benadrukt om patiënten te ondersteunen in hun keuze voor behandelopties. In het tweede deel wordt de noodzaak van gespecialiseerde revalidatie na een totale laryngectomie benadrukt, met speciale aandacht voor stemprotheses (SP) en Heat and Moisture Exchangers (HME, ook wel kunstneus). Stemprotheses zorgen ervoor dat patiënten weer kunnen leren spreken, alhoewel ze een beperkte levensduur hebben wat zorgt voor ongeplande ziekenhuisbezoeken voor een stemprothese wissel. HMEs verwarmen en bevochtigen de luchtweg en verminderen hierdoor longklachten. Echter hebben ze een vaste ademweerstand, waardoor bijvoorbeeld tijdens intensief bewegen, patiënten het gevoel hebben dat ze te weinig lucht krijgen. Dit kan ertoe leiden dat men de HME minder draagt.

Deel 1: Gedeelde besluitvorming in hoofd hals kanker

Hoofdstuk 2 is een systematische review met meta-analyse, die de huidige literatuur onderzoekt over het voorkomen van 'beslissingsconflicten' (decisional conflict = DC) en 'beslissingsspijt' (decisional regret = DR) bij mensen met hoofd-halskanker. Er is niet veel onderzoek naar gedaan en de onderzoeken die er gedaan zijn variëren in samenstelling van patiëntengroep, tumorlocatie, stadium en de gebruikte vragenlijsten. Uit de gevonden literatuur bleek dat een significant percentage van de patiënten te maken heeft met beslissingsspijt en -conflict. De bevindingen wijzen op een dringende noodzaak voor betere voorlichtingsstrategieën en beslissingshulpmiddelen om patiënten te ondersteunen bij hun behandelkeuzes. We vonden geen duidelijke verschillen tussen patiënten met verschillende tumorlocaties en tumor stadia.

In **hoofdstuk 3** is de huidige stand van de geobserveerde en ervaren gedeelde besluitvorming (SDM) onder hoofd-halschirurgen, patiënten en hun familieleden binnen ons eigen instituut onderzocht. We hebben de ervaren niveaus van SDM en patiëntbetrokkenheid gemeten met behulp van vragenlijsten en de geobserveerde SDM geanalyseerd door audiogesprekken van consultaties te bestuderen. Uit onze resultaten bleek dat chirurgen en patiënten de mate van SDM overschatten in vergelijking met de werkelijke observaties. Ondanks dat de ervaren SDM-scores hoog waren, waren de geobserveerde scores gemiddeld. Er was een positieve associatie tussen de duur van de consultaties en de geobserveerde SDM-score van chirurgen. Onze bevindingen suggereren dat er meer aandacht moet worden besteed aan de doelen, waarden en voorkeuren van patiënten tijdens consultaties om de kwaliteit van SDM te verbeteren.

In **hoofdstuk 4** is onderzocht of patiënten met gevorderde larynx kanker, die als behandeling kunnen kiezen tussen een strottenhoofd sparende behandeling of het operatief verwijderen ervan, beide behandelopties met aanzienlijke impact op hun levenskwaliteit en met een verschil in overleving. Uit de studie bleek dat na de voorlichting bijna alle deelnemers (98%) een significant niveau van besluitvormingsconflict ervoeren. Daarnaast toonden de resultaten aan dat de kennis over de behandelopties laag was, waarbij patiënten gemiddeld slechts 47% van de kennisvragen correct beantwoordden. Dit gebrek aan begrip, vooral over laryngectomie, benadrukt de noodzaak voor verbeterde patiëntenvoorlichting, ondanks dat zowel patiënten als artsen een redelijk niveau van gedeelde besluitvorming meldden.

Hoofdstuk 5 is het vervolg van hoofdstuk 4. Hierin is onderzocht wat de invloed van een door ons ontwikkelde keuzehulp (PDA) zou zijn op patiënten met gevorderd larynxcarcinoom. De groep die de PDA gebruikte, vertoonde minder besluitvormingsconflict en meer kennis in vergelijking met de groep die de standaardprocedure volgde (hoofdstuk 4). Zij ervoeren meer gedeelde besluitvorming. Hieruit blijkt dat het gebruik van een PDA bijdraagt aan een effectievere besluitvorming bij patiënten met gevorderde larynxkanker, door zowel het conflict tijdens het besluitvormingsproces te verminderen als de kennis en ervaring van gedeelde besluitvorming te verbeteren.

Hoofdstuk 6 beschrijft de ontwikkeling van een PDA, voor patiënten met orofarynxkanker die in aanmerking komen voor een genezende operatie of bestraling. Met behulp van internationale normen en methoden zoals diepte-interviews en sessies waarin artsen en patiënten hardop hun gedachtes uitspreken is deze keuzehulp ontworpen om de behandelopties duidelijk uit te leggen. Deze keuzehulp is uitgebreid geëvalueerd en aangepast met input van zowel patiënten die de ziekte overleefd hebben als

medische specialisten, wat resulteerde in een gebruiksvriendelijk en informatief hulpmiddel. De keuzehulp geeft een duidelijk overzicht van de verschillen in korte- en langetermijneffecten tussen chirurgie en bestraling, en wordt gewaardeerd om zijn helderheid en nuttige bijdrage aan het besluitvormingsproces. Hiermee biedt het patiënten en artsen ondersteuning bij het maken van weloverwogen behandelkeuzes.

Deel 2: Rehabilitatie na een totale laryngectomie

In **hoofdstuk 7** is onderzocht of het preventief vervangen van stemprotheses, stemprothese-lekkages bij patiënten na een TL kan voorkomen. Deze lekkages beïnvloeden de kwaliteit van leven van patiënten negatief en leiden tot onverwachte ziekenhuisbezoeken. Als doel wilden we kijken of we 70% van de lekkages kunnen voorkomen door preventief te wisselen. We analyseerden gegevens van patiënten die tussen 2000 en 2012 waren behandeld in het Nederlands Kanker Instituut. Onze resultaten toonden aan dat er grote variatie is in de levensduur van de stemprotheses, zowel tussen en binnen patiënten, wat betekent dat het preventief vervangen van prothesen vaak onpraktisch is. Voorspellen van de levensduur is hierdoor erg moeizaam, en daardoor ene preventief wisselmoment ook. Rekenkundige simulaties lieten zien dat het voorkomen van 70% van de lekkages door profylactische vervanging niet haalbaar is. Dit suggereert dat deze strategie vanwege de grote variabiliteit in de levensduur van de stemprotheses niet mogelijk is.

Hoofdstuk 8 beschrijft de testresultaten van de nieuwe Provox Vega High Performance (PVHP) stemprothese, die is ontworpen voor een langere en meer voorspelbare levensduur. Er werd onderzocht hoe patiënten de PVHP ervoeren, eventuele bijwerkingen, stemkwaliteit en de levensduur. Patiënten die eerder een andere stemprothese gebruikten (zoals de Provox Vega of ActiValve Light), konden worden geïncludeerd in deze studie. Van de vijftien deelnemers accepteerde 87% de PVHP na twee weken, maar dit daalde tot 40% nadat de stemprothese was gaan lekken er een wissel moest plaatsvinden. De mediane levensduur van de PVHP was 64 dagen. De stemkwaliteit verschilde niet tussen de PVHP en de standaard prothese. De meest gemelde bijwerking was kleverigheid van het PVHP-ventiel (46%). De acceptatie van een nieuwe stemprothese hangt sterk af van de levensduur, die momenteel nog een uitdaging blijft.

In **hoofdstuk 9** is onderzocht of maximale cardiopulmonale inspanningstesten (CPET) bij patiënten na een laryngectomie haalbaar zijn met een Heat-and-Moisture-Exchanger (HME) in situ, met behulp van een speciaal ontworpen connector. Daarnaast verkenden we het effect van verschillende HME-weerstanden op de inspanningscapaciteit van deze groep. Tien deelnemers ondergingen twee CPET's met de HME die zij dagelijks

gebruiken (met verschillende weerstanden) en één speciaal ontwikkeld voor intensievere inspanning (hele lage weerstand), waarbij de volgorde willekeurig en geblindeerd was. Alle deelnemers voltooiden beide tests zonder bijwerkingen. Slechts vier deelnemers bereikten een Respiratory Exchange Ratio (RER) >1.1 in ten minste één test. De maximale inspanningsniveaus verschilden niet bij gebruik van HMEs met verschillende weerstanden. Hoewel CPET met een HME haalbaar is, lijkt het protocol niet geschikt om de maximale inspanningscapaciteit van deze groep te bereiken. Een andere bevinding is dat het verlagen van de HME-weerstand de inspanningscapaciteit in deze groep niet verhoogd.

Hoofdstuk 10 deelt het inspirerende verhaal van een laryngectomiepatiënt die, ondanks de ingrijpende operatie, opnieuw heeft leren zingen en gitaar spelen. Na zijn totale laryngectomie begon de patiënt met stemrehabilitatie en leerde snel stemprothese spraak en handenvrij spreken. Zijn passie voor zingen leidde tot het opzetten van een YouTube-kanaal waarop hij video's deelt van Nederlandse liedjes en Franse chansons. Dit verhaal toont hoe zingen na een totale laryngectomie niet alleen de ademhalingsfunctie en stemkwaliteit kan verbeteren, maar ook de levenskwaliteit en het zelfvertrouwen van patiënten vergroot. Het benadrukt de waarde van muziek en zang als revalidatiehulpmiddel en als bron van vreugde.

In **hoofdstuk 11** worden alle bovengenoemde hoofdstukken bediscussieerd en in context met elkaar geplaatst. Dit proefschrift richt zich op het verbeteren van de zorg voor hoofd- en halskanker door gedeelde besluitvorming (SDM) en verscheidene aspecten van revalidatie na een TL te onderzoeken.

Kijkend naar de toekomst, onderstreept hoofdstuk 11 de noodzaak van verdere ontwikkeling en verfijning van SDM-praktijken. Er is een gebrek aan onderzoek in dit veld terwijl deze patiënten ingrijpende en levens veranderende behandelingen ondergaan en SDM hen veel kan bieden. Voor revalidatie tools zou toekomstig onderzoek zich moeten richten op het verbeteren van de duurzaamheid en gebruiksvriendelijkheid van stemprothesen. Technologische innovaties, zoals kunstmatige intelligentie, kunnen een rol gaan spelen in het bevorderen van gedeelde besluitvorming en het personaliseren van revalidatieprogramma's. Deze stappen kunnen toekomstig patiënten ondersteunen in hun traject en potentieel hun kwaliteit van leven te verbeteren.


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2020	Medical statistics in Oncology, NKI-AvL Amsterdam
2020	Global Postlaryngectomy Rehabilitation Academy, NKI-AvL Amsterdam
2020	Good Clinical Practice, NKI-AvL Amsterdam
2020	Clinical Research in the Netherlands – Legislation & Procedures, Paul Janssen Futurelab Leiden (LUMC)
2020	Getting ready with Castor EDC, Castor
2021	Statistical Methods, ACTA
2021	Scientific writing and presenting, ACTA
2021	BROK locale meeting, NKI-AvL Amsterdam
2021	Webinar EORTC H&N Young Investigators Group Webinar
2021	AHNS webinar: TORS
2021	R-statistics, NKI-AvL Amsterdam
2021	BROK course
2021	Scientific integrity, NKI-AvL Amsterdam

Conferences and presentations

	Conferences/meetings	**Presentation**
2019-2024	Dutch ENT meeting	Posters, orals
2020	NWHHT research group, Utrecht	Oral
2020	Patient society Head-and-neck oncology, Utrecht	Oral
2021	International PhD Student Cancer Conference (digital)	-
2021	AHNS (digital)	Poster
2021	MKA lustrum conference, Breda	Oral
2021	NWHHT congres, Nijmegen	Oral
2022	ICHNO-ECHNO, Brussels	Poster

Conferences and presentations (Continued)

	Conferences/meetings	Presentation
2022	OOA-retreat, Amsterdam	Poster
2022	ENTER-dag, Amsterdam	-
2022	IAOO, Chicago	Oral
2022	NWHHT, Groningen	Oral
2022	ICHNO, Barcelona (digital)	Oral
2022	Tumorboard Leeds (digital)	Oral
2022	Research meeting Atos, Malmö	Oral
2023	ECHNO, Lissbon	Oral
2023	IFHNOS, Rome	Orals
2023	AHNS, Montreal	Oral, poster
2023	NWHHT, Rotterdam	Oral
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2024	Third place Outstanding publication by the International Shared Decision Making Society

Dankwoord

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About the author

Anne Heirman, born on the first of October 1993, in Groningen, is the eldest of three children. She completed her secondary education at the Gymnasium Aletta Jacobs College in 2012, and started her studies in Medicine at the University of Groningen. During her studies, Anne was actively involved in student life, participating in a sorority, committees, and sports. She completed clinical rotations at the University Medical Center Groningen (UMCG) and Deventer Ziekenhuis, and undertook a tropical medicine internship in northern Mozambique.

Anne completed her final year of medical school at the Department of Otolaryngology and Head and Neck Surgery at the UMCG. After graduation, she was granted a PhD position at the Department of Head and Neck Oncology at the Netherlands Cancer Institute, under the supervision of Prof. Van den Brekel, Dr. Halmos, Dr. Van der Molen, and Dr. Dirven, with a subsequent opportunity to begin her residency in Otolaryngology at the UMCG.

Anne began working at the Netherlands Cancer Institute in October 2019 and commenced her PhD in January 2020. Her research involved clinical studies with laryngectomized patients and the development of decision aids for head and neck oncology patients, requiring collaboration with developers, medical professionals, and language specialists. Anne presented her findings at several international conferences. On May 1, 2024, she began her residency in Otorhinolaryngology at the UMCG.

Anne is deeply interested in the human in all its aspects, which fueled her research in head and neck oncology—a field that profoundly impacts patients' quality of life. Her passion for medicine and research also led her to complete a Master's in Evidence-Based Practice in Healthcare, earning her the title of clinical epidemiologist.

Outside of her professional life, Anne has a love for the outdoors and has traveled when possible, exploring countries such as Australia, New Zealand, Thailand, Malaysia, Indonesia, Mozambique, Canada, the United States, Mexico, Belize, and South Africa.

She lives in Meerstad with her partner, Sam, and their daughter, Nore.