

Hamilton DW, Bins JE, McMeekin P, Pedersen A, Steen IN, DeSoyza A,  
Thomson RT, Paleri V, Wilson JA.

[Quality compared to quantity of life in laryngeal cancer: A time trade-off study.](#)

*Head and Neck* 2016, 38(S1), E631-E637

**Copyright:**

This is the peer reviewed version of the following article: Hamilton DW, Bins JE, McMeekin P, Pedersen A, Steen IN, DeSoyza A, Thomson RT, Paleri V, Wilson JA. [Quality compared to quantity of life in laryngeal cancer: A time trade-off study.](#) *Head and Neck* 2016, 38(S1), E631-E637, which has been published in final form at <http://dx.doi.org/10.1002/hed.24061>. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Self-Archiving.

**DOI link to article:**

<http://dx.doi.org/10.1002/hed.24061>

**Date deposited:**

07/09/2016

**Embargo release date:**

01 April 2017

Choose a building block.

## Quality compared to quantity of life in laryngeal cancer: A time trade-off study

David W. Hamilton, PhD,<sup>1\*</sup> Janneke E. Bins, MBBS,<sup>2</sup> Peter McMeekin, PhD,<sup>1</sup> Ami Pedersen, MBBS,<sup>3</sup> Nicholas Steen, PhD,<sup>1</sup> Anthony De Soyza, PhD,<sup>4,5</sup> Richard Thomson, MD,<sup>1</sup> Vinidh Paleri, FRCS,<sup>3</sup> Janet A. Wilson, MD<sup>3</sup>

<sup>1</sup>Institute of Health and Society, Newcastle University, Newcastle upon Tyne, United Kingdom, <sup>2</sup>Jeroen Bosch Hospital, Hertogenbosch, The Netherlands, <sup>3</sup>Freeman Hospital, Newcastle upon Tyne, United Kingdom, <sup>4</sup>Institute of Cellular Medicine, Respiratory Medicine, Newcastle University, Newcastle upon Tyne, United Kingdom, <sup>5</sup>Respiratory Medicine Freeman Hospital, Newcastle upon Tyne, United Kingdom.

Accepted 27 March 2015

Published online 00 Month 2015 in Wiley Online Library (wileyonlinelibrary.com). DOI 10.1002/hed.24061

**ABSTRACT:** *Background.* The purpose of this study was to use time trade-off to assess the factors influencing patients' decisions in advanced laryngeal cancer. Time trade-off is a well-established method of assessing how individuals value a particular health state.

*Methods.* We developed vignettes depicting life after chemoradiotherapy or laryngectomy. One hundred fourteen participants ranked them, assigned utility values, and rated the importance of survival on treatment choice.

*Results.* Chemoradiotherapy was preferred by 62% and laryngectomy by 38%. Chemoradiotherapy optimal outcome had the highest mean utility value (0.64) followed by total laryngectomy optimal outcome (0.56). Total

laryngectomy poor outcome (0.33) was equivalent to chemoradiotherapy poor outcome (0.32). The average survival advantage required for a participant to change their preferred choice was 2.1 years.

*Conclusion.* The functional treatment outcome had a greater effect on health state utility values than treatment modality. In many individuals, larynx conservation may not be the primary consideration in treatment preference. © 2015 Wiley Periodicals, Inc. *Head Neck* 00: 000–000, 2015

**KEY WORDS:** chemoradiotherapy, head and neck neoplasms, laryngeal neoplasms, laryngectomy, larynx

### INTRODUCTION

Treatment options for locally advanced laryngeal cancer have changed radically over the past 2 decades.<sup>1–3</sup> In 1981, when total laryngectomy was the standard of care, McNeil et al<sup>4</sup> published a landmark study scrutinizing the trade-off between quantity and quality of life faced by patients diagnosed with locally advanced laryngeal cancer. At the time of its publication, the majority of patients undergoing a total laryngectomy would have no voice after the procedure, or would produce a voice using an electrolarynx, which gives a characteristically artificial or robotic sound. The premise of the utility analysis McNeil presented to her 37 healthy volunteers was that radiotherapy was associated with a poorer survival, but a better voice outcome, whereas a laryngectomy achieved an improved survival at the expense of an artificial voice. The conclusion that survival may not be the most

important outcome for all patients has been cited over 600 times in subsequent literature, but is typically misquoted to support the move toward primary nonsurgical therapy of locally advanced laryngeal cancer.<sup>5</sup>

McNeil's demonstration that not everyone valued survival at any price became incorporated into clinical management. Since McNeil's study, large randomized controlled trials have been interpreted as showing that radical courses of chemoradiotherapy offered equivalent survival to total laryngectomy.<sup>6,7</sup> As a result, concurrent chemoradiotherapy has become accepted as the first-line management for locally advanced laryngeal cancer, with total laryngectomy relegated to a salvage intervention. This practice has recently been questioned, however, because of concerns about the high complication rate, the need for excision of necrotic larynx, and, most worryingly, the possibility that overall survival from advanced laryngeal cancer has been adversely affected.<sup>1,8</sup> This is the first study to revisit McNeil's seminal time trade-off experiment using modern treatment outcomes. We aimed to reevaluate the preferences of a population demographically matched to the head and neck cancer population and to assess the importance of survival on treatment choice.

### MATERIALS AND METHODS

#### Participants

Participants were aged over 45 years, with no history of head and neck cancer. All participants were able to

\*Corresponding author: D. Hamilton, Institute of Health and Society, Baddiley Clark Building, Newcastle University, NE2 4AX, Newcastle upon Tyne, UK. E-mail: David.hamilton@ncl.ac.uk

Contract grant sponsor: This article presents independent research funded by a National Institute of Health Research (NIHR) Doctoral Research Fellowship. The views expressed are those of the author(s) and not necessarily those of the National Health Service, the National Institute for Health Research, or the Department of Health.

This work was presented orally at the North of England ENT Society 2013; and orally at the British Association of Head and Neck Oncologists 2013.

speak or read English. Patients were recruited from 2 cohorts: healthy volunteers and patients with chronic obstructive pulmonary disease (COPD). Patients with COPD were recruited from a registry at the Sir William Leech Respiratory Clinical Trials Unit, Freeman Hospital, Newcastle upon Tyne, UK, and outpatient clinics. These patients were recruited as they have similar characteristics to the head and neck cancer population; for example age, smoking status, comorbidity profile, and socioeconomic class. Healthy volunteers were recruited from diverse sources to ensure laryngeal cancer population age/sex representation, including from VOICENorth (a registry held by the Clinical Aging Research Unit at Newcastle University), control registries at the Sir William Leech Respiratory Clinical Trials Unit, spouses of patients with COPD, and a public advertisement.

All participants were interviewed between January 2011 and December 2012, after they provided written informed consent. The study was approved by both the Newcastle University Ethics Committee and Newcastle upon Tyne Regional Ethics Committee and adopted onto the UK National Institute for Health Research portfolio (UKCRN ID 10996).

Four health state descriptors were developed depicting the treatment process and outcome for chemoradiotherapy optimal outcome, chemoradiotherapy with complications, total laryngectomy optimal outcome, and total laryngectomy with complications. The health state vignettes were initially compiled by members of the study team (J.B. and D.H.) using extensive literature review and clinical experience. They were then shown to surgeons, oncologists, speech and language therapists, and clinical nurse specialists and edited based on the feedback received. Finally, the health state vignettes were shown to patients who had undergone treatment (surgical and nonsurgical) to determine whether they were a true reflection of life after treatment for head and neck cancer and again edited based on the feedback. Audio and video recordings of speech after chemoradiotherapy and of tracheo-esophageal speech after total laryngectomy were developed during pilot work to use alongside the vignettes, together with pictures of a tracheal stoma, skin changes because of radiotherapy, and a gastrostomy.

First, participants were presented with the audiovisual information on the process and outcomes of treatment using the videos, recordings, and pictures developed during the pilot work together with a standardized explanation given by the interviewer. The 4 health states were then introduced and participants were asked to carry out 3 exercises. In exercise 1, participants ranked the 4 available health states alongside their own health from most to least desirable. In exercise 2, participants were offered a choice between alternative 1 (to remain in one of the health states for 10 years) and alternative 2 (to retain normal health, but with a decreased survival [x years]). X was varied until the respondent became indifferent between the 2 alternatives, at which point the utility value for that health state was derived. For example, a participant who felt 10 years with a laryngectomy was equivalent to 7 years in their normal health state yields a laryngectomy utility value of  $7/10 = 0.7$ . Each of the 4 health states was presented similarly and in a random

TABLE 1. Sociodemographic descriptors of participants.

	No. of participants	%
Participant type		
COPD patient	63	45
Control	51	55
Sex		
Male	56	49
Female	58	51
Home situation		
Alone	42	39
Family	66	61
Smoking status		
Nonsmoker	37	32
Ex-smoker	57	50
Smoker	20	18
Educational level		
Secondary school	51	47
Certificate/diploma	41	38
University	16	15

Abbreviations: COPD, chronic obstructive pulmonary disease.

order to control for order of study bias.<sup>9</sup> During exercise 3, the participants were asked again which of the 2 optimal outcome health states they would prefer: total laryngectomy optimal outcome, or chemoradiotherapy optimal outcome. The years of survival associated with the non-preferred option were then increased (using a similar technique to the time trade-off exercise) in order to determine the number of years of survival advantage, if any, that would lead to a change in their decision.

### Statistical analysis

We calculated that 70 participants would be needed to detect a difference in mean utility scores of 0.1 on the interval scale, in which  $\alpha = 0.05$ , power = 80%, and  $SD = 0.25$  were around the mean score. The minimum meaningful utility value difference is difficult to define, however, a difference of 0.1 is considered to be clinically significant.<sup>9</sup> Differences in health utilities ascribed to various health states were investigated using mixed models with variation within participants (each participant rated a number of health outcomes), and variation between participants included as random effects. Participant type (patient or control), treatment modality (chemoradiotherapy or total laryngectomy), and treatment outcome (optimal or poor) were included as fixed effects. To test whether the difference between optimal and poor outcomes differed between treatment modalities, an interaction between treatment modality and treatment outcome was included in the model. Models were fitted using the “xtreg” procedure in Stata version 12 using maximum likelihood estimation.

### RESULTS

A total of 114 participants took part in the study, including 63 patients with COPD and 51 healthy volunteers. The average age of participants was 67.3 years (Table 1). One participant was able to complete only the ranking exercise.

The chemoradiotherapy optimal outcome was chosen as the preferred health state by 71 of 114 participants (62%).

TABLE 2. Summary of how favorably each health state was ranked.

Health state	Rank ordering (%)*			
	1	2	3	4
TL good	43 (37.7)	51 (44.7)	23 (20.2)	–
TL poor	–	16 (14.0)	53 (46.5)	42 (36.8)
CRT good	71 (62.3)	26 (22.8)	16 (14.0)	–
CRT poor	–	21 (18.5)	22 (19.3)	72 (63.2)

Abbreviations: TL, total laryngectomy; CRT, chemoradiotherapy.  
 \*The most preferable health state is ranked as 1 and the least preferable is ranked as 4.

Total laryngectomy with good outcome was the preferred health state for 43 of 114 (38%; Table 2). The majority of patients (72 of 114; 63%) ranked chemoradiotherapy with complications as their least preferred health state.

A utility value is a value between zero and 1, in which zero is assumed to be equated to “being dead” and 1 is equated with “full/normal health.”<sup>10</sup> The difference in utility value considered to be clinically significant is 0.1. The observed distributions of utility scores for each treatment modality and outcome are shown in Figures 1 and 2. The utility associated with different outcomes was investigated by fitting a series of mixed models. The interaction between treatment modality (chemoradiotherapy vs total laryngectomy) and treatment outcome (optimal vs poor) was highly significant ( $p < .001$ ).

When all patients’ data were combined, chemoradiotherapy optimal outcome had the highest mean utility

value (0.64; 95% confidence interval [CI] = 0.58–0.69) followed by total laryngectomy optimal outcome (0.57; 95% CI = 0.51–0.63; Figure 2). The mean difference between total laryngectomy optimal outcome and chemoradiotherapy optimal outcome was 0.07 (95% CI = 0.02–0.12). However, when the utility values for optimal outcome and outcome with complications health states were combined for each of the treatment modalities, there was minimal difference between total laryngectomy and chemoradiotherapy (mean, 0.03; 95% CI = –0.01 to 0.06). When patients were divided according to their ranking in exercise 1, those who ranked total laryngectomy the highest assigned a higher utility value to total laryngectomy optimal outcome than chemoradiotherapy optimal outcome (0.59 vs 0.53; Table 3). Total laryngectomy poor outcome was not significantly different to chemoradiotherapy poor outcome with a difference of 0.02 (95% CI = –0.06 to 0.3). The difference between optimal outcome and outcome with complications was greater for chemoradiotherapy (0.32; 95% CI = 0.27–0.37) than for total laryngectomy (0.23; 95% CI = 0.19–0.28).

There was a large variation in the survival advantage required to switch participant choice from their preferred treatment to their nonpreferred treatment modality. Thirty-six participants (32%) would not change their initial preference for any survival advantage. Of the 68% willing to consider a change, the mean survival advantage required to change was 2.5 years (range, 6 months to 5 years). A higher ratio of patients who ranked total laryngectomy as their first choice (37%) would never change

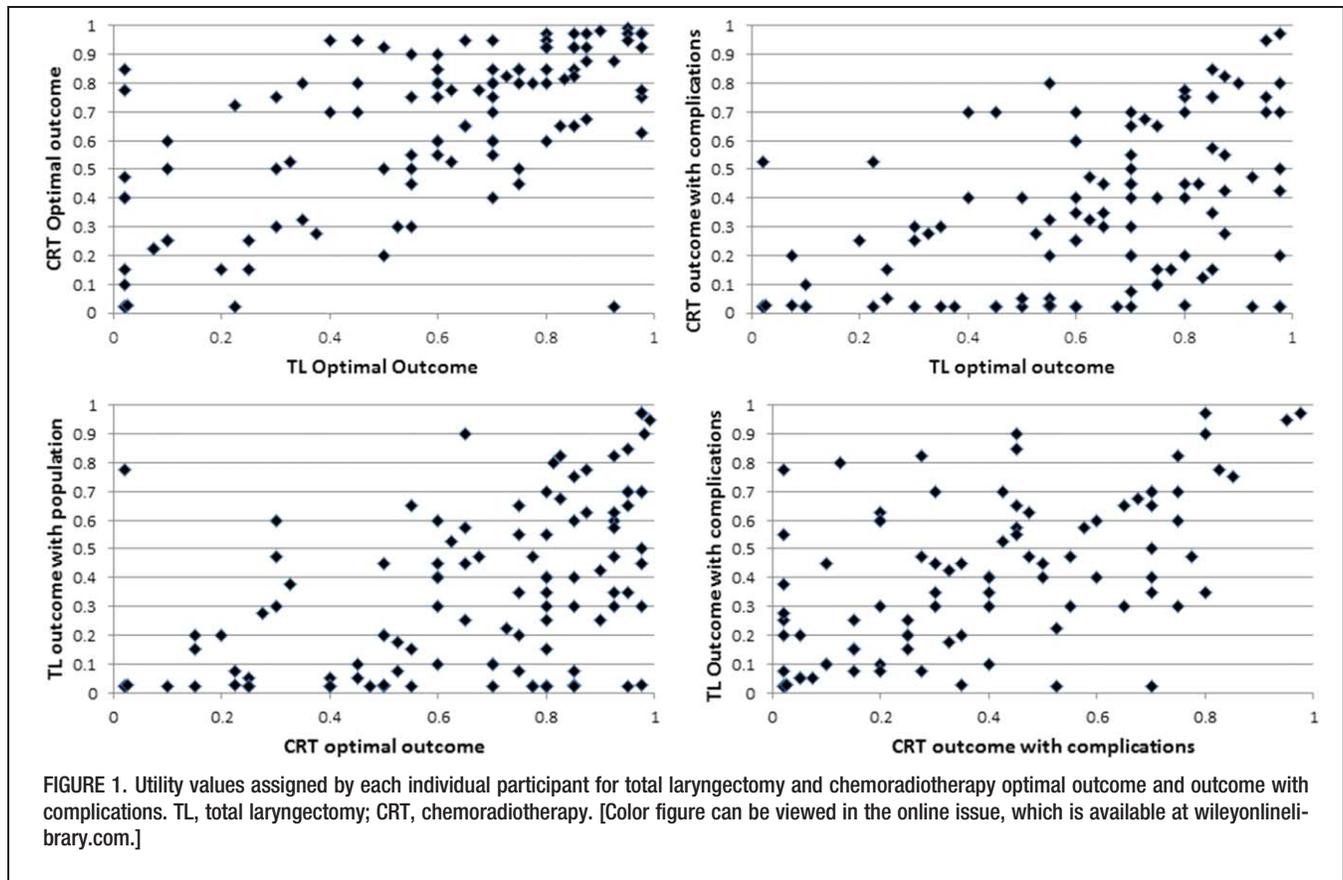
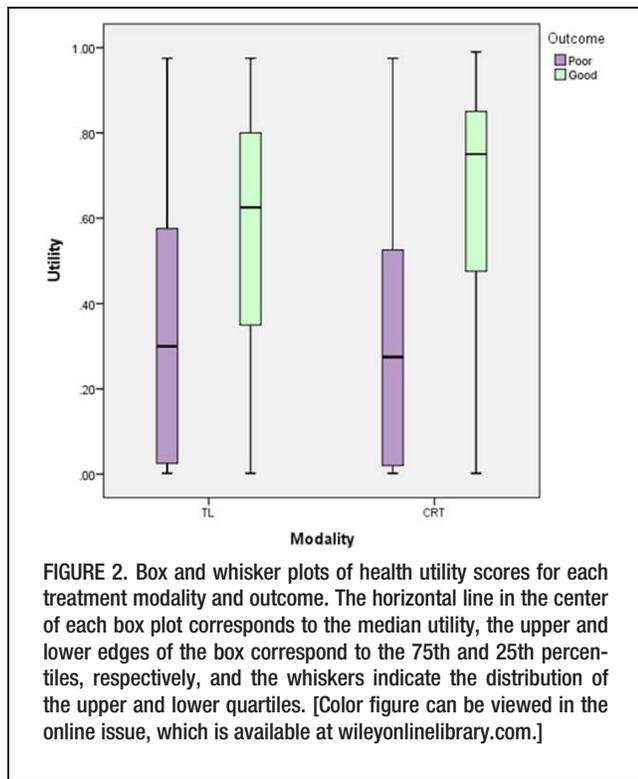


FIGURE 1. Utility values assigned by each individual participant for total laryngectomy and chemoradiotherapy optimal outcome and outcome with complications. TL, total laryngectomy; CRT, chemoradiotherapy. [Color figure can be viewed in the online issue, which is available at [wileyonlinelibrary.com](http://wileyonlinelibrary.com).]



their decision compared to those who ranked chemoradiotherapy as the first choice (24%).

## DISCUSSION

This is the first study to critically appraise treatment choices for the locally advanced laryngeal cancer population demographically matched to new attenders at a head and neck cancer clinic. The chemoradiotherapy optimal outcome was the most preferred health state with 62% of participants ranking it highest, although a significant minority of participants (38%) would rank total laryngectomy with optimal outcome first. The functional outcome of treatment was a greater determinant of the value of assigned health state utility than treatment modality. Chemoradiotherapy had the larger difference between optimal outcome and outcome with complications and, as a result, 63% of participants ranked chemoradiotherapy outcome with complications as the least preferred option. If the utility values for both good and bad outcomes were combined for each modality, there was no significant difference between them. In addition, on average, those who ranked a treatment modality as preferable (in exercise 1) subsequently assigned the associated health state a higher utility value. Participants held their preferences strongly, with almost a third of participants adhering to their original treatment choice, despite being offered a significant survival advantage for their nonpreferred option. Those who chose total laryngectomy as their first option were more likely to adhere to this option than those who chose chemoradiotherapy.

The desire to preserve the larynx has driven clinical trial design for 25 years, under the assumption that this is a priority for patients. Our data question this central prin-

TABLE 3. Average utility values assigned using time trade-off, divided by patients ranking total laryngectomy and those ranking chemoradiotherapy the highest in exercise 1.

	CRT optimal outcome	CRT outcome with complications	CRT optimal outcome	CRT outcome with complications
Ranked CRT first	0.70	0.37	0.55	0.34
Ranked TL first	0.53	0.22	0.59	0.22
All participants	0.64	0.31	0.57	0.33

Abbreviations: CRT, chemoradiotherapy; TL, total laryngectomy.

ciple, and suggest that the potential trade-offs that may be required to preserve the larynx are not acceptable to all patients. Indeed, it was recognized recently by the International Head and Neck Scientific Group that “avoiding surgery at the expense of losing the ability to swallow and/or speak with other modes of therapy cannot be considered a success,”<sup>11</sup> leaving the head and neck cancer community to ponder whether the pendulum has swung too far in favor of chemoradiotherapy.<sup>12</sup>

Various authors have used expected utility theory to address the question of treatment choice in locally advanced laryngeal cancer. Laccourreye et al<sup>13</sup> recently asked 309 otolaryngology patients the reduction in cure rate that they would accept in order to preserve their larynx. The presented trade-off, however, was predicated on a reduced chance of cure from nonsurgical management, which was unacceptable to 24.6% of participants. In this study, the authors described the health states according to modality but did not attempt to characterize the quality of the options presented or define the presence or absence of complications. Jalukar et al<sup>14</sup> rated the importance of outcome with regard to specific aspects of quality of life (breathing, eating, speech, etc.), but these were not modality specific. The study by van der Donk et al<sup>15</sup> used time trade-off to assess T3 laryngeal cancer outcomes and reported utility values that were similar to our own (0.73 for radiotherapy and 0.66 for surgery). In the van der Donk et al<sup>15</sup> study, brief favorable outcome descriptors were presented; in the present study these descriptors were accompanied by audio and visual information.

There is disagreement about which population provides the best valuation of a health state. Patients who have experience with a health state may be thought to provide the most “accurate” assessment of its quality, but tend to rate it higher than those who have not.<sup>16</sup> The United Kingdom’s National Institute for Health and Clinical Excellence<sup>17</sup> clearly states that the health state descriptors should be informed by patients and valued by a representative sample of the population. In 1981, McNeil’s sample population consisted of firemen and middle managers, which arguably did not sufficiently represent patients with head and neck cancer.<sup>4</sup> The present study participants match patients who present as new attenders to a head and neck cancer clinic. Health state descriptors were developed in conjunction with patients experiencing the health state and health professionals involved in the care of these patients, and our sample population was demographically matched to the head and neck cancer population.

Shared decision-making allows the sharing of information between the patient and the clinician. The clinician provides information about the risks and benefits of the treatment options, and the patient provides information about their values and preferences.<sup>18</sup> We have demonstrated that participants with similar age and educational level to those attending the head and neck cancer clinic are capable of processing complex information about treatment choices and expressing strong preferences as a result. Participants ranked treatment options and weighed up a complex (albeit hypothetical) treatment choice: the resultant choice had a significant effect on the utility value assigned to health states.

Thirty years ago, McNeil et al<sup>4</sup> concluded that survival may not be the priority for all patients treated. Our conclusion has an important difference: larynx preservation may not be the priority of all patients and therefore patient preference should be a central part of the treatment selection. Our study has demonstrated that the quality of the treatment outcome had a more significant effect on the utility value assigned to a health state than the modality of treatment. Research is therefore required on the relative proportion of good versus poor outcome as this emerges as a key consideration for appropriate patient participation in decision-making.

## APPENDIX

### HEALTH STATE: Total laryngectomy optimal outcome

- Voice
  - You will lose your normal speech.
  - You will produce a voice by putting a finger on the hole in your neck, pushing air out through your mouth.
- Temporary side effects
  - Pain after operation will be well controlled with painkillers.
  - Radiotherapy after the operation will give you burned red skin in the neck.
  - After the operation, you will have difficulty swallowing, this will improve gradually.
- Permanent side effects
  - You will have a changed appearance – there will be a hole in the neck (covered by a speech button).
  - Your sense of smell and taste will be affected or lost.
  - You will produce some mucus from the hole in the neck.
- Function
  - In time, you will be able to eat a near normal to normal diet.
  - You are likely to have a relatively good voice using the speech valve.

### HEALTH STATE: Total laryngectomy outcome with complications

- Voice
  - You will lose your normal speech.
  - You will produce a voice by putting a finger on the hole in your neck, pushing air out through your mouth.
- Temporary side effects
  - Pain after operation will be well controlled with painkillers.
  - Radiotherapy after the operation will give you burned red skin in the neck.
  - After the operation, you will have difficulty swallowing, this will improve gradually.
- Permanent side effects
  - You will have a changed appearance – there will be a hole in the neck (covered by a speech button).
  - Your sense of smell and taste will be affected or lost.
  - You will produce some mucus from the hole in the neck.
- Function
  - You may need to stick to a softened diet, because of swallowing difficulties.
  - You may struggle to use the speech valve or to produce a good voice, if so, you may need to find other ways to communicate like gestures or writing things down.
- Complications

- The wound in your neck may not heal correctly.
- There might be irritation and crusting of the hole in the neck.
- Depending on the severity of complications, you may need further operations on your neck.

### HEALTH STATE: Chemoradiotherapy optimal outcome

- Voice
  - You will be able to speak normally, but your voice will sound weaker and hoarse.
- Temporary side effects
  - The treatment will make you feel fatigued and ill.
  - You will experience difficulty and pain while swallowing and, therefore, may need a feeding tube through the nose or into the stomach.
  - Red skin reaction and swelling of the neck may be painful.
- Permanent side effects
  - You will have a dry mouth.
  - Your ability to taste food might change.
- Function
  - You will be able to have a near normal diet.
  - Your voice will be different than before.

### HEALTH STATE: Chemoradiotherapy outcome with complications

- Voice
  - You will be able to speak normally, but your voice will sound weaker and hoarse.
- Temporary side effects
  - The treatment will make you feel sick, fatigued, and ill, which may cause you to be admitted to the hospital.
  - You will experience difficulty and pain while swallowing and, therefore, will need a feeding tube through the nose or into the stomach.
  - You will have a painful skin reaction and swelling of the neck, which may need regular morphine medication.
- Permanent side effects
  - You will have a very dry mouth, which will bother you during the biggest part of the day.
  - Your ability to taste food will change or be lost.
- Function
  - Swallowing will cause problems, because liquids may go down the wrong way and you may be advised to have nothing by mouth. This means you will be fed by a feeding tube.
  - You might struggle to be heard when there are more people in a room.
- Complications
  - You will have thick secretions in your throat that are difficult to clear and may cause trouble breathing.
  - A feeding tube in the stomach (percutaneous endoscopic gastrostomy), this is likely to be permanent.
  - There will be 1 or 2 large, painful ulcers in the mouth.

### REFERENCES

1. Olsen KD. Reexamining the treatment of advanced laryngeal cancer. *Head Neck* 2010;32:1–7.
2. Grégoire V, Jeraj R, Lee JA, O'Sullivan B. Radiotherapy for head and neck tumours in 2012 and beyond: conformal, tailored, and adaptive? *Lancet Oncol* 2012;13:e292–e300.
3. Haddad R, O'Neill A, Rabinowits G, et al. Induction chemotherapy followed by concurrent chemoradiotherapy (sequential chemoradiotherapy) versus concurrent chemoradiotherapy alone in locally advanced head and neck cancer (PARADIGM): a randomised phase 3 trial. *Lancet Oncol* 2013;14:257–264.
4. McNeil BJ, Weichselbaum R, Pauker SG. Speech and survival: tradeoffs between quality and quantity of life in laryngeal cancer. *N Engl J Med* 1981;305:982–987.
5. Vokes EE, Weichselbaum RR, Lippman SM, Hong WK. Head and neck cancer. *N Engl J Med* 1993;328:184–194.
6. Forastiere AA, Goepfert H, Maor M, et al. Concurrent chemotherapy and radiotherapy for organ preservation in advanced laryngeal cancer. *N Engl J Med* 2003;349:2091–2098.
7. [No authors listed]. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. The Department of Veterans Affairs Laryngeal Cancer Study Group. *N Engl J Med* 1991;324:1685–1690.
8. Hoffman HT, Porter K, Karnell LH, et al. Laryngeal cancer in the United States: changes in demographics, patterns of care, and survival. *Laryngoscope* 2006;116(9 Pt 2 Suppl 111):1–13.
9. Furlong W, Feeny D, Torrance G, Barr R, Horsman J. Guide to design and development of health state utility instrumentation. Centre for Health

- Economic and Policy Analysis: McMaster University, Hamilton, Ontario; 1990.
10. Drummond MF. Methods for the economic evaluation of health care programmes. 2nd ed. Oxford, UK: Oxford University Press; 1997.
  11. Strojjan P, Haigentz M Jr, Bradford CR, et al. Chemoradiotherapy vs. total laryngectomy for primary treatment of advanced laryngeal squamous cell carcinoma. *Oral Oncol* 2013;49:283–286.
  12. Holsinger FC, Weber RS. Swing of the surgical pendulum: a return to surgery for treatment of head and neck cancer in the 21st century? *Int J Radiat Oncol Biol Phys* 2007;69(2 Suppl):S129–S131.
  13. Laccourreye O, Malinvaud D, Holsinger FC, Consoli S, Ménard M, Bonfils P. Trade-off between survival and laryngeal preservation in advanced laryngeal cancer: the otorhinolaryngology patient's perspective. *Ann Otol Rhinol Laryngol* 2012;121:570–575.
  14. Jalukar V, Funk GF, Christensen AJ, Karnell LH, Moran PJ. Health states following head and neck cancer treatment: patient, health-care professional, and public perspectives. *Head Neck* 1998;20:600–608.
  15. van der Donk J, Levendag PC, Kuijpers AJ, et al. Patient participation in clinical decision-making for treatment of T3 laryngeal cancer: a comparison of state and process utilities. *J Clin Oncol* 1995;13:2369–2378.
  16. Post PN, Stiggelbout AM, Wakker PP. The utility of health states after stroke: a systematic review of the literature. *Stroke* 2001;32:1425–1429.
  17. NICE. Guide to the methods for technology appraisal. London, UK: National Institute for Health and Clinical Excellence, 2008.
  18. Elwyn G, Frosch D, Thomson R, et al. Shared decision making: a model for clinical practice. *J Gen Intern Med* 2012;27:1361–1367.