Practice of laryngectomy rehabilitation interventions: a perspective from Europe/the Netherlands

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Practice of Laryngectomy Rehabilitation Interventions:
A perspective from Europe/the Netherlands

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Abstract

Purpose of Review
Total laryngectomy rehabilitation (TLR) in Europe is not uniform, with quite some differences in approach and infrastructure between the various countries. In e.g. the Netherlands, Switzerland, Scandinavia, and more recently also in the UK, Head and Neck Cancer treatment and rehabilitation shows a high level of centralisation in dedicated HNC centres. In other European countries, the level of centralisation is lower, with more patients treated in low-volume hospitals. This paper focuses on the situation in the Netherlands, and where applicable, will discuss regional variations in Europe.

Recent Findings
Prosthetic surgical voice restoration (PSVR) presently is method of choice in Europe, and use of oesophageal and electrolarynx voice has moved to the background. In most European countries (except UK and Ireland), PSVR is physician driven, with an indispensable role for Speech Language Pathologists, and increasingly for oncology nurses. Indwelling voice prostheses are mostly preferred, also because these devices can be implanted at the time of tracheo-oesophageal puncture. Pulmonary rehabilitation is achieved with heat and moisture exchangers, which, based on extensive clinical and basic physiology research, are considered an obligatory therapy measure. Besides PSVR, also issues such as smoking cessation, dysphagia/swallowing rehabilitation, and olfaction/taste rehabilitation are discussed. Especially the latter has shown great progress over the last decade, and is another example of increasing implementation of evidence-based practice in TLR.

Summary
TLR has shown considerable progress over the last decades, and through the intensified collaboration between all clinicians involved, significantly has improved vocal, pulmonary, and olfactory rehabilitation after TL.

Keywords
Total laryngectomy; voice rehabilitation; pulmonary rehabilitation; olfactory rehabilitation; swallowing rehabilitation; multidisciplinary approach

Bullet list
- Prosthetic Surgical Voice Restoration is the method of choice for re-establishing postlaryngectomy oral communication, ensuring early regain of optimal voice and speech quality
- As with any surgical method, adverse events have to be taken into account, but clinical research has shown that the majority of these are easily manageable, especially through optimal collaboration between multidisciplinary rehabilitation team members (e.g. head and neck surgeon, speech language pathologist, and oncology nurse)
- Oesophageal and electrolarynx voice rehabilitation should not be neglected since both methods offer practical alternatives in case prosthetic voice is temporarily ‘out of order’
- Pulmonary rehabilitation with heat and moisture exchangers (HMEs) to compensate for the short-circuited upper respiratory tract function is an essential ‘Level-I evidence-based’ therapy measure for all laryngectomized patients, irrespective of voice restoration method; in most European countries healthcare authorities have acknowledged the benefits of HMEs and thus are reimbursing these medical devices
- Olfactory rehabilitation by means of the Nasal Airflow Inducing Manoeuvre (‘Polite Yawning’) is an effective method for restoring the impaired sense of smell after total laryngectomy and should be integrated in every postlaryngectomy rehabilitation programme

Introduction

Worldwide there is an increasing interest in head and neck cancer (HNC) and total laryngectomy rehabilitation (TLR), as is underlined in recent publications about the potential role of the WHO's International Classification of Functioning, Disability and Health (ICF) in this area. E.g. Eadie et al. and Tsieschner et al. showed that the ICF can provide a conceptual framework for assessing and treating individuals with HNC-related communication disorders. However, unlike in many other areas of rehabilitative medicine, where a structured multidisciplinary team approach forms the basis, such a team in HNC, consisting of head and neck surgeon, speech pathologist, oncology nurse, dietician, physical therapist, occupational therapist, psychosocial worker, psychologist, and rehabilitative specialist, is still quite rare. There are some exceptions, e.g. in Germany and France, but rehabilitation centres there often are functioning quite isolated from HNC centres. In the Netherlands Cancer Institute (NCI) this ‘void’ has been addressed through development of an evidence-based multidisciplinary HNC rehabilitation programme. This programme, including TLR, recently has been acknowledged by the healthcare authorities as a genuine multidisciplinary rehabilitation programme, which therefore now is structurally financed and can be implemented in the HNC centres participating in the Dutch Head and Neck Society (DHNS; www.nwhht.nl).

TLR in Europe is not as uniform as maybe anticipated from a non-European perspective. There are some differences in approach and infrastructure between various countries. In the native country of the authors, HNC treatment and rehabilitation shows a high level of centralisation in dedicated HNC centres, mainly in academic hospitals and the NCI. These centres are collaborating in the DHNS, which over the past 15 years has developed evidence-based consensus reports on all major HNC topics, starting with larynx cancer. Also for example in Switzerland and Scandinavian countries, most HNC patients are treated in a limited number of (academic) hospitals, and in the UK, following the Calman Hine Report (1995), centralisation of HNC also has increased. In other European countries, the level of centralisation is lower, with more patients treated in low-volume hospitals. Providing comprehensive information here of all specific TLR aspects in Europe would be too elaborate, and therefore focus will be on the situation in the Netherlands, and where applicable, comparison with other countries will be made.
Healthcare insurance and total laryngectomy care
The Netherlands has a privatized healthcare system with compulsory healthcare insurance of all citizens. In case patients receive social security benefits, insurance premium is included in that support. For TLR in the recent past Speech Language Pathology (SLP) care in the standard healthcare insurance was somewhat limited, but this has improved since 2010 after recognition of the afore-mentioned HNR programme. Possibilities in other European countries vary, e.g. with socialized medicine taking care of TLR in the UK and Spain, and various degrees of privatization levels in other countries.

With respect to medical devices applied in TLR, these are part of the standard healthcare insurance and reimbursement for e.g. voice prosthesis (VP), heat and moisture exchanger (HME), automatic tracheostoma valve (ASV), adhesive patches, and tracheostoma cannula, does not pose a problem thus far. In European countries this situation is similar (e.g. Scandinavian countries, Croatia, Switzerland, UK), or there are limitations, such as an annual ceiling (e.g. Germany, Belgium), or reimbursement for some and not all relevant medical devices (VP yes, HME no; e.g. Poland).

In most European countries, except UK and Ireland, the physician is leading in the physical (after-) care of TL patients, as far as choice and handling of the VP is concerned, while SLP and oncology nurse are responsible for all other aspects of voice and speech rehabilitation, including teaching daily maintenance of all above-mentioned medical devices. After the initial treatment and rehabilitation all patients remain in follow-up, and since Prosthetic Surgical Voice Restoration (PSVR) is the norm in the Netherlands, most TL patients remain in follow-up for the rest of their live. Mostly this follow-up is provided in the HNC centre.

Since in the Netherlands, most TL patients are treated in comprehensive HNC centres, the initial TLR is provided by SLPs, HN oncology nurses, and the other allied health clinicians in those centres. Also during follow-up TLR is mostly provided in the centre, and only rarely in the community, also because patient numbers are rather limited. In the Netherlands (almost 17 million inhabitants), the annual incidence of larynx cancer is approximately 700 (with approximately 150 TLs), and the total TL population is approximately 2000. Like in many other European countries, there is an active, well-organized patient society for laryngectomées (http://www.nsvg.nfk.nl). This society is very supportive and can provide also well-trained patient counsellors, who routinely counsel patients scheduled for TL.

Smoking cessation programme
In the consensus reports of the DHNS, providing a smoking cessation programme in every centre is recommended, but thus far such programme has not yet been implemented everywhere. In a recent report, also the Dutch ENT society has stressed the importance of a smoking cessation programme, and has prioritized this in their planning. The validity of this recommendation is underlined by the positive results of the smoking cessation programme in the NCI, with a cessation rate of 33% at one-year. For other substance abuse, e.g. alcohol, treatment often is more complicated, and counselling and psychosocial support groups are available either in-
house or in the community.

**Dysphagia rehabilitation**

Swallowing problems of laryngectomees are not in the forefront of the attention of their caregivers although they are not uncommon, i.e. changes in dietary consistency and habits are reported in 25-50% of patients. 6,7 Careful assessment of swallowing (and speech) function with videofluoroscopy (VF) is key in dysphagia diagnosis and treatment. This is especially important when dysphagia is caused by pharyngoesophageal stenosis, occurring in up to 20% of both primary and in salvage laryngectomies. 8 Regular dilatation of such a stenosis is often needed, and in exceptional cases partial pharyngeal reconstruction, with a flap used as a patch, or a complete circumferential reconstruction, might be the only solution to regain oral intake. Another reason for dysphagia, diagnosed with VF is a pseudo-epiglottis, also called a pseudo-vallecula. This is a pouch formed at the base of tongue, which is seen more often in case of a vertical closure of the pharyngeal defect. Signs are swallowing difficulties, regurgitation, halitosis, and a ‘wet’ voice. Once diagnosed, treatment consists of endoscopic removal of the scar band at the base of tongue.

No specific swallowing rehabilitation programmes for laryngectomized patients have been described yet, and based on careful VF-evaluation, swallowing exercises by the SLP often have to be individualized. 9

**Smell/taste rehabilitation**

Loss of (passive) sense of smell is yet another obvious consequence of the disconnection of the upper and lower respiratory tracts, and the relevance of olfaction for taste is well known. Tracheostoma breathing precludes passage of breathing air along nasal olfactory epithelium and thus of ‘registration’ of odour molecules, essential for normal passive sense of smell. The extent of the postlaryngectomy olfaction problem studied in a series of 63 patients, showed that two-thirds of the patients failed the olfaction tests while one-third passed. 10 This latter group (called ‘smellers’) reported better sense of smell in daily life, fewer disturbances in taste, and better appetite. Correlating olfaction test results with observations of what patients were doing while performing the tests, ‘smellers’ were using muscles in face and neck more actively than ‘non-smellers’. This lead in 2000 to discovery of the Nasal Airflow Inducing Manoeuvre (NAIM), also called ‘Polite Yawning’ manoeuvre, since the latter describes the feeling well: enlarging the oral cavity by lowering the jaw and keeping the lips closed and the soft palate relaxed. 11,12 In subsequent intervention studies, the effectiveness of this method for olfaction rehabilitation was proven. Since then, studies in Sweden and Australia have confirmed efficacy of the NAIM and thus have given this rehabilitation method ‘level I evidence status’. 13,14 Since the discovery of the NAIM, rehabilitation of the sense of smell by the SLP is fully implemented in the TLR programme, has gained widespread acceptance in the Netherlands, and is increasingly used in other European countries. 15-18

**Psychosocial support and intervention**

Psychosocial support (PS) and on indication interventions always have been an integral part of the care in the HNC centres in the Netherlands, as most likely also in the rest of Europe. Especially in view of the high incidence of alcohol and tobacco abuse in HNC patients this is an
essential part of the treatment and after care. PS now also is fully integrated in the HNR programme, and because of the regular (weekly) multidisciplinary meetings can be optimally geared with the rest of the team/programme activities.

**Voice and speech rehabilitation**

Voice and speech rehabilitation traditionally have been the most prominent intervention aspect in total laryngectomy aftercare. For many decades, oesophageal and electrolarynx voicing have been the mainstay for restoring oral communication, but over the last two to three decades this has shifted to prosthetic tracheoesophageal voice.

**Tracheoesophageal voice**

The preferred method of restoring postlaryngectomy communication is PSVR. The DHNS-consensus report states: “Primary insertion of an indwelling voice prosthesis is the method of choice for postlaryngectomy voice rehabilitation.” There are very few exceptions to this advice, and even in case of salvage surgery after (chemo-) radiotherapy, most patients will receive an indwelling VP through primary tracheoesophageal puncture (TEP) and immediate VP implantation. The PSVR method as originally described by Singer and Blom, inserting a TEP stenting catheter, and delaying insertion of a non-indwelling VP until 10–12 days postoperatively, never gained support in the Netherlands, and also not in most European countries besides the UK and Ireland. Indwelling VPs thus are preferred, not only because these devices are suitable to be implanted immediately after TEP, but also because in general maintenance is easier and learning curves are shorter than with non-indwelling VPs, despite the fact that the replacement of an indwelling device always is a matter for the clinician. A recent new disposable puncture set, based on the Seldinger technique, further has improved this preferred primary TEP concept. Secondary TEPs are less frequent and mainly applied after extensive pharyngeal reconstruction, e.g. gastric pull-up, or in case re-puncture is required.

**Oesophageal voice**

Oesophageal voice (OV) rehabilitation, still a valuable technique, has moved to the background. OV has a long track record, with major contributions from the Netherlands by Molenaar-Bijl and Damsté, but extensive research has shown that in comparison with TE voicing, especially volume, fluency, and phonation duration are inferior. Therefore, its decreased popularity is understandable, but nevertheless, it would be good, when patients were encouraged more to additionally acquire this in principle ‘handsfree’ speech mode. This maybe could be stimulated some time after TL, when TE voice and speech are well established, and patients often are in a better psychological and physical condition. There is some evidence that once good TE voice has been acquired, OV is easier to acquire as well, keeping in mind the technical differences between the two methods (initiating voice with pulmonary airflow versus injection of air into the oesophagus first before voicing can start).

**Electrolarynx voice**

For electrolarynx voice (EV) the same holds true as for OV in the Netherlands. Its acceptance always has been low, much lower than e.g. in the UK and USA, because of its unnatural
monotonous sound. Nevertheless, also this method should be considered a useful back up in case TE voicing is (temporarily) ‘out of order’. In view of the fact that also this device is fully reimbursed in many countries, there is certainly much in favour for teaching EV as well.

**Voice prosthesis adverse events: incidence and management**

Adverse events in PSVR at present are essentially still similar to what has been published some 10 years ago. VPVs do not have an eternal device life and require regular replacement, mainly because the VP is rapidly contaminated and overgrown with a biofilm (consisting of bacteria and yeasts). This biofilm deteriorates the material and cause incompetence of the valve and thus internal leakage. This is not a (medical) adverse event, and the main reason for VP replacement (approximately 80%). In a subcategory (15%) of patients this internal leakage occurs very frequently, and for these patients the solution is a specialize VP, which uses tiny magnets to obtain an active closure of the valve.29-31

The second reason for VP replacement/adjustment is peripheral leakage. Normal healing processes cause a gradual decrease of the surgical oedema at the TEP site, and the subsequent shortening of the TEP tract makes the VP too long. This issue is simply corrected by inserting a shorter VP (about 10% of all VP changes), and if this solves the problem, this ‘natural’ shortening of the TEP is not considered an adverse event.28 However, when simple downsizing does not solve peripheral leakage, this should be considered a complication. A fairly recent solution for this is application of a thin silicone washer behind the tracheal flange, which solves mild peripheral leakage in the vast majority of cases, at least temporarily, until a more definitive solution is chosen.32 A second option here is to apply a purse string suture.33 A third option is to augment the TEP tract with e.g. injectable silicone or autologous fat.34,35 Ultimately, in rare cases, surgical closure of the TEP tract might be unavoidable. This approach to peripheral leakage actually forms an algorithm with the subsequent options: 1 downsizing if applicable; 2 washer application; 3 purse string suture; 4 tissue augmentation; 5 surgical closure. Temporary VP removal allowing the TEP to shrink for some days is another, not attractive option, because this requires a feeding tube and a cuffed cannula, which is not very appealing to patients. Massive TEP enlargement occurs very seldom, but that adverse event can be a considerable burden for patient and HN team. However, discussing the surgical solutions is out of the scope of this review. Sometimes, however, these large TEPs can be handled by a VP with an enlarged flange, which either can be ordered commercially,36 or can be made in-house, as is the case in the NCI.

A third category of adverse events is formed by local inflammatory TEP/tissue reactions, which are mainly treated with broad-spectrum antibiotics, and elimination of the pressure of the VP flanges on the mucosa by inserting a longer VP if necessary. It should be stressed here that there is increasing evidence that gastro-oesophageal reflux disease (GERD) plays a major role in this TEP reaction.37-39 This means that proton-pump inhibitors, adequately dosed, do play an important role in the treatment of this problem. Also peripheral leakage caused by TEP tract widening often is attributable to GERD, according to the above cited studies, and not to prosthesis diameter, as once postulated,40 but now disproved.41,42 Together, peripheral leakage, not responsive to simple downsizing, and local inflammatory reactions form the remaining 10%
of adverse event/replacement indications.

Impact of recent clinical research evidence and new developments on local practice in PSVR

The best example of what impact clinical research evidence has had on the current SLP practice in TLR is the research on postlaryngectomy PSVR. Whereas until 20–30 years ago, OV rehabilitation was the norm, this has completely changed since the early nineties of the last centuries. Although until then only a few Dutch HNC centres had fully implemented PSVR, all remaining centres in the mean time have changed their TLR practice according to the consensus recommendations of the DHNS. Also the above-mentioned solutions for adverse events have been explored in many clinical studies, and thus can be implemented as evidence-based practice. Another example is the evidence-based programme developed by van Rossum et al. 43, in which deficits in TL speech, such as decreased voiced-voiceless distinction, specifically are addressed. This programme comprises of two parts, the first consisting of articulation training on specific phonemes, and the second of teaching clear speech and optimal prosody (phrasing and use of accent). This programme has shown to be effective in a small patient series, 44 and although more evidence of its usefulness in larger patient cohorts is desirable, it is increasingly implemented in the present rehabilitation programme.

Outcomes reporting

Systematic collection of outcome data is still not common practice in TLR, but certainly is something that should be pursued much more in the coming years. Patient reported outcomes (PROs), e.g. through standard validated structured questionnaires, so far mainly have been used in research projects, and have not (yet) been implemented widely in every day practice. There are positive developments, however, in this respect, with the nationwide implementation of the ‘Distress meter’ now on its way in the Netherlands. This validated PRO gives patients the possibility to indicate on a scale from one to ten (visualised as a thermometer) how much ‘distress’ was experienced in the past week with respect to physical, emotional, social, and practical well being.

The recent development of the HNR programme has made it possible to collect more data about participating TL patients as well. Standardized voice and speech recordings are now regularly made, and used for monitoring progress over time, also contributing to a growing database for research. As part of the HNR programme, other PRO’s (EORTC C30 and HN35) are now used to record Quality of Life (QoL) pre- and posttreatment, and most likely will play a more prominent role in the near future in reporting about QoL changes/improvements. Moreover, regular evaluation of specific rehabilitation goals, an integral part of the HNR programme, also improves insight in various TLR aspects, also giving multidisciplinary team members better insight in what other team members achieve and how that relates to their own patient advancement.

Economic aspects

Budgetary constraints are present in all HNC centres, but so far, no requirements for cost-effectiveness analyses of established clinical treatment tools are required. However, this is certainly something that increasingly will be requested in the near future. The understandably growing pressure to only apply evidence-based practice tools is the main reason for this. As
already mentioned, all TLR costs for patients in the Netherlands, so far, are fully reimbursed by the healthcare insurance, including all necessary tools for daily maintenance. The fact that the effectiveness of all these devices has been proven in prospective clinical trials is quite helpful. More cost-effectiveness oriented analyses however certainly will be needed in the near future. An example of such an analysis is the recent evaluation of the cost-effectiveness of a preventive rehabilitation programme in patients with advanced head and neck cancer treated with concomitant chemoradiotherapy (CRT). This analysis revealed that the applied rehabilitation programme indeed improved long term outcome with a reduction of dysphagia related problems at a cost of roughly € 3200 per QALY (Quality Adjusted Life Year). With a threshold of € 20,000 per QALY for rehabilitation-related treatment programmes, this preventive programme was considered cost-effective, and thus could be implemented. Studies like this will lead to implementation of effective programmes, but certainly also can lead to abandoning non-effective or questionable clinical methods.

Pulmonary rehabilitation

Pulmonary rehabilitation after total laryngectomy is another essential facet of TLR. Clinical and physiology research has shown that the short-circuiting of the upper respiratory tract has significant consequences for the pulmonary system. For instance, during normal nasal breathing in living-room conditions (22°C, and 40% relative humidity, which equals an absolute water content of 8mg H2O/L), air-temperature at the subglottic level has increased to 32°C, and humidity has quadrupled to 35-36mg H2O/L. In the alveoli, temperature is 37°C and relative humidity 100% (an absolute humidity of 44mg H2O/L). This means that air-temperature and humidity in the stoma are significantly lower than at the subglottic level, which impair cilia function and mucus transport in the trachea. Restoring this lost upper respiratory tract air-conditioning capacity presently best can be achieved with a heat and moisture exchanger (HME). Clinical research has shown that these HMEs significantly reduce pulmonary side effects of TL, such as involuntary coughing, excessive phlegm production, and forced expectoration for clearing the trachea from mucous. In parallel with the improved pulmonary status, a significant improvement in several quality of life aspects, and also in voice quality has been demonstrated. HMEs obviously should be applied 24/7, irrespective of voice rehabilitation method. For patients with a voice prosthesis airtight occlusion of the stoma, when covered with a HME, is essential, and peristomal adhesive patches and special laryngectomy canulas and buttons allow the vast majority of patients to apply a HME successfully.

Factors influencing type and timing of pulmonary rehabilitation offered

Since clinical and basic physiology research has provided level I evidence that HMEs can compensate for a major part for the lost humidifying by the upper respiratory tract, this means that HMEs should be considered an obligatory therapy/rehabilitation measure for all TL patients. In many European countries healthcare authorities have acknowledged this and, therefore HMEs are reimbursed in the majority of them. The actual choice of what HME suites which patient best is still not easy, but for several devices in vitro and in vivo data are available, which indicate their humidifying capacity, even under different climatological circumstances. Recent studies have shown that the humidifying capacity of the newer generation HMEs
considerably has improved, making these devices presently the HME of choice, certainly in the Netherlands.\textsuperscript{60}

In many HNC centres in the Netherlands, and increasingly e.g. in Germany and France, HMEs have replaced postoperative external humidification, and are already applied immediately after the surgery. A recent randomized controlled clinical trial, comparing heated external humidification with the immediate application of a HME, showed that HMEs lead to a much higher compliance, significantly less mucus production, need to suction the trachea, and patient satisfaction.\textsuperscript{61} Moreover, there was a significant reduction of nursing time and daily costs, which makes immediate postoperative application of an HME the method of choice also for the early postoperative period. This means that besides SLPs also nursing-staff plays an important role in this patient counselling and teaching. As with VPs, where nurses teach patients how to clean the device already during the hospital stay, during that period they also train patients in proper application of adhesives (or cannulas) and HME cassettes. An obvious other advantage of this early exposure to HMEs is that patients consider this medical device as an integral part of their aftercare, which has shown to increase compliance.\textsuperscript{62} As a consequence, after patient’s discharge from the hospital, use of (homecare) external humidifiers is mostly abandoned in the Netherlands, although that is still surprisingly popular in other European countries.

**Economic aspects**

In the Netherlands, the implementation of immediate postoperative HME use in the hospital is quite easy, because for hospital administrations, reduced nursing time and material costs are convincing arguments, even outweighing proven clinical benefits. However, proper analysis of differences in costs always should be done at the national/local level, because of frequently varying costs for various components of each system. As with VPs, costs for pulmonary rehabilitation for laryngectomized patients in the Netherlands are fully reimbursed, including all necessary tools for HME application, e.g. adhesives and cannulas/buttons. Again, the fact that these devices all have proven their efficacy in prospective clinical trials has been quite helpful to achieve this.\textsuperscript{55} Cost-effectiveness studies are currently underway, and although results are not in yet, it is expected that these studies will show a relatively low cost per QALY, because of gain in QoL, and of reduction of pulmonary infections,\textsuperscript{50} lowering need for antibiotics. An interesting thought in this respect is that the well-known wintertime trachea-bronchitis with often severe, sometimes even life-threatening crusting is a disease of the past in the Netherlands. Many other health care providers in ‘endemic-HME’ countries also have experienced this.

**Conclusion**

Comprehensive multidisciplinary rehabilitation after total laryngectomy, including vocal, pulmonary, olfactory, and swallowing rehabilitation, has evolved substantially over the last decades, substantially decreasing long-term morbidity of this still often unavoidable surgical procedure and significantly benefitting quality of life of laryngectomized individuals.

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A well-described and conducted RCT showing that rehabilitation of the sense of smell after total laryngectomy with the nasal airflow inducing maneuver can be speeded up with an intensified rehabilitation program.


These authors for the first time have quantified the nasal airflow achieved with the nasal airflow inducing maneuver: most patients can reach a flow of 100 ml/second, which is well above the olfaction threshold of 60 ml/second.


A long overdue study showing that also with the Blom-Singer indwelling voice prosthesis primary TEP with immediate fitting of the prosthesis is a reliable method, a technique used with other indwelling devices already for decades.


A landmark study on the significance of gastroesophageal reflux for TEP complications and reduced device life, and the importance of adequate treatment with PPIs to solve these issues.


This systematic literature review and meta-analysis shows that the postulated impact of voice prosthesis diameter on TEP complications can be relegated to the realm of fiction.


A well-conducted retrospective study also showing that voice prosthesis diameter is not the postulated factor relevant for TEP complications.


One of the first studies on cost-effectiveness analysis of a new treatment modality, a methodology becoming increasingly important in this era of evidence-based medicine.


The first RCT showing the significant advantages of immediate postlaryngectomy use of an HME over the application of a heated-external humidifier for pulmonary protection and rehabilitation, not only with respect to clinical effects, compliance and patient satisfaction, but also in terms of (reduced) nursing time and cost-effectiveness.