CDA-AMC Health Technology Review

Voice Prostheses and Heat-Moisture Exchangers for Adults following Total Laryngectomy: An updated Rapid Review

March 2025

Rapid Review

Abbreviations

ASC	alternative stoma cover
BS-LP	Blom-Singer low pressure
CI	confidence interval
EV	esophageal voice
GRADE	grading of recommendations, assessment, development, and evaluations
HME	heat moisture exchanger
ICER	incremental cost effectiveness ratio
SF-36	36-Item short form survey instrument
QALY	quality-adjusted life years
QOL	quality of life
TEP	tracheoesophageal puncture
TEV	tracheoesophageal voice
VHI	voice handicap index
VP	voice prosthesis

Key Messages

What is the issue?

- Total laryngectomy is a surgical procedure that removes the larynx. During the surgery, the trachea is diverted to an opening in the neck called a stoma. This change in breathing pattern is permanent, significantly impacting the ability to swallow, breathe, and, speak, greatly impacting overall quality of life.
- Post-laryngectomy interventions include olfactory, voice, swallowing rehabilitation and addressing the psychosocial aspects of patient recovery. Voice rehabilitation is an important aspect of post-laryngectomy care to restore vocal communication. The use of an esophageal voice, an artificial larynx (electrolarynx), and a tracheoesophageal voice with voice prosthesis are options for restoring voice communication in adults following total laryngectomy.
- The population of patients in Canada undergoing total laryngectomy is relatively small. There is reported to be well established clinical care for post-laryngectomy voice rehabilitation, yet the current evidence is limited. A request for a review of the evidence to inform policy decisions related to voice prostheses (indwelling and non-indwelling devices) and heat moisture exchangers for adults following total laryngectomy was submitted to CDA-AMC.

What did we do?

- This report is now posted for public feedback. This is an update of a rapid review report published in October 2024, which includes 1 additional systematic review and extends the rapid review methodology to include engagement of clinical specialists and the lived experience of patients following a laryngectomy.
- We aimed to identify and summarize related evidence and recommendations from systematic reviews, health economic evaluations and evidence-based guidelines with a contextual evaluation of clinical and patient experience. The clinical research questions were co-developed with the project requestor.
- We searched journal databases and grey literature for relevant evidence published since January 2019. We used 5-year search period for this review considering the identified systematic reviews had searched earlier periods. Three patients were interviewed to gain insight on their experience using these devices. 1 Speech and Language Pathologist with experience working with patients following laryngectomy provided clinical expert review of the draft report.

What did we find?

- The use of voice prostheses and heat and moisture exchangers for adults following total laryngectomy is reported by clinicians to be common practice across Canada. Both patients and the speech and language pathologist who reviewed this report underscore the importance of these devices in supporting voice restoration, pulmonary rehabilitation, preventing infection, and improving quality of life following surgery.
- 9 eligible publications were identified including: 5 systematic reviews, 3 economic evaluations, and 1 evidence-based guideline. Owing to various methodological limitations, confidence in the evidence identified was determined to be very low.
- 3 patients reported that using voice prostheses and heat moisture exchangers after total laryngectomy is critical to their ability to communicate, maintain independence, and prevent lung infection. Whilst there are challenges with maintaining the devices and additional costs for the supplies needed to support use, the benefits of these devices were seen to outweigh these challenges.
- 2 systematic reviews compared tracheoesophageal voice using voice prostheses with esophageal voice. While 1 systematic review reported that tracheoesophageal voice with voice protheses may have a more positive impact on quality-of-life measures, while 1 systematic review found no-statistically significant differences in voice handicap index and voice-related quality of life. The speech and language pathologist who reviewed this report highlighted the difficulty associated with learning esophageal voice compared to voice prostheses. One of our patient partners agreed with this and mentioned they had not encountered patients within their community who used esophageal voice exclusively.
- 1 systematic review with network meta-analysis compared 10 voice prostheses (8 indwelling and 2 non-indwelling). This review did not compare indwelling and non-indwelling devices as two distinct groups. Critical methodological flaws with this systematic review were identified. Most comparisons between various VPs showed no statistically significant differences in device replacements, device lifetime, airflow resistance, leakage, speech rate, maximum phonation time, patient device preference, phonatory effort, fundamental frequency, voice loudness, speech intelligibility, stoma stenosis, dislodgement, fistula problems, granulation, prosthesis inaccurate size, prosthesis deterioration and survival rate. Many effect estimates were imprecise, i.e., the confidence intervals were wide, including the potential that either of the devices being compared could be favoured.

- 1 systematic review reported that using heat and moisture exchangers compared to no heat and moisture exchangers, significantly improved several clinical outcomes including mucus production, coughing, forced expectorations, the number of days requiring chest physiotherapy after surgery, tracheobronchitis or pneumonia episodes and improved patient satisfaction.
- No evidence regarding cost-effectiveness of voice prostheses versus no prostheses, indwelling versus non-indwelling prostheses, or comparisons among different non-indwelling prostheses for adults following laryngectomy was identified. Heat moisture exchangers were reported as cost-effective compared to alternative stoma covers from U.S. perspectives. These findings may not be generalizable to Canada.
- 1 evidence-based guideline developed in Spain recommended replacing the prosthesis with a double-flanged one, such as Provox XtraSeal, adjusting the diameter and length, or placing a silicone sheet (or ring) on the tracheal side of the prosthesis can be used to manage periprosthetic leakage. Our review did not identify any evidence-based guidelines regarding the use of HME for adults following total laryngectomy.

What does it mean?

- The clinical and patient community we engaged with consider voice protheses and heat and moisture exchangers essential devices. The evidence base related to their benefit and cost effectiveness is limited. The perspectives of speech and language pathologists working with patients, and patients with lived experience with these devices, may supplement decision-making by contextualizing the evidence currently available.
- Decisions regarding the choice of voice prostheses should consider patient's tracheoesophageal puncture (TEP) shape and size, patients' values and preferences, accessibility, affordability, and other factors such as physical and mental capabilities, caregiver support, and patient motivation.
- While the evidence is limited, patients and clinicians report that adding heat moisture exchangers could be beneficial in several clinical outcomes, such as mucus reduction, infection prevention and reported patient satisfaction.
- Future systematic reviews should be planned and conducted in alignment with recognized methodological standards and should be transparently reported. As the certainty of evidence from high quality systematic reviews relies, in part, on the risk of bias of their included studies, future primary studies should aim to draw from developed patient registries.

Context and Policy Issues

What is a total laryngectomy?

A laryngectomy is a surgical procedure involving the partial or total removal of the larynx.[1,2] A total laryngectomy is indicated for several reasons, including neck injuries, or, for advanced squamous cell carcinomas of the larynx or hypopharynx that have not metastasized distantly.[2,3] In Canada, from 2003 to 2007, approximately 900 new laryngeal cancer cases were diagnosed in males and 195 in females, representing roughly 1.1% and 0.3% of all new cancer cases, respectively.[4] The total laryngectomy procedure impacts a patient's ability to swallow, breathe, speak, and necessitates breathing through a surgically created stoma. Following surgery, there is a need for specialized care and rehabilitation to restore essential functions.[5,6]

Post-laryngectomy interventions include olfactory, voice, swallowing rehabilitation and addressing the psychosocial aspects of patient recovery.[7-9] For patients who have undergone laryngectomy, interdisciplinary collaboration and personalized care plans are essential to optimize outcomes and improve the quality of life.[7,8] Voice rehabilitation is an important aspect of post-laryngectomy care to restore vocal communication. Ensuring sufficient heat and moisture to the airway, often using heat and moisture exchangers, is also important as the disconnection of the upper and lower airways results in the loss of natural conditioning of inhaled air (humidification, filtration, and heating), which may support improved patient outcomes.[10-12]

What are commonly used approaches for voice restoration?

The commonly used approaches to restore voice and communication for total laryngectomee patients include: esophageal voice, an artificial larynx (electrolarynx), or tracheoesophageal voice restoration using a voice prothesis.[13] Successful voice restoration has a wide-ranging positive effect, improving quality of life, enhancing employment prospects, strengthening family relationships, and facilitating access to essential services.[14,15]

Esophageal voice involves introducing and expelling air from the esophagus to produce sound.[13] Esophageal voice provides the benefit of hands-free verbal communication without the need for devices.[13] Esophageal voice, where air is "swallowed" or "injected" and then "released or burped" for voice production, differs from lung-powered voice. Due to a limited air supply, it is often quieter, requires more effort, and has reduced utterance length than a lung-powered voice.[16,17] The esophageal voice often has a lower pitch and a "wet" quality, which can reduce intelligibility.[16] Anatomical-physiological, patient-related, treatment and rehabilitation-related factors could impact a patient's ability to use esophageal voice effectively.[18] Mastering esophageal voice can be difficult, often requiring 4 to 6 months or more to achieve proficiency. Furthermore, there is a significant shortage of skilled esophageal voice trainers, and less than 30% of patients use esophageal voice as their primary method of communication.[13]

The electrolarynx is a widely used, battery-powered device used for voice, offering communication. However, it has a mechanical sound and typically requires one-hand operation.[13] To achieve more natural-sounding speech, some modern electrolarynx models offer pitch features.[13] Choosing the best electrolarynx requires careful consideration of factors such as sufficient sound transfer to ensure clear speech and the individual's personal preference.[13] In the Veterans Administration Cooperative Study, involving 166 patients following laryngectomy, 55% primarily used an artificial electrolarynx and 31% primarily used tracheoesophageal speech for speech production.[13]

Tracheoesophageal voice (TEV) restoration, either performed during (primary tracheoesophageal puncture, TEP) or after (secondary TEP) laryngectomy, provides the most comparable speech alternative to natural, fluent speech and ease of production.[13] Typically, TEV with voice prosthesis is reported to have better voice quality and intelligibility than esophageal voice and electrolarynx voice.[19] However, TEV with voice prostheses demands considerable time to learn and financial resources.[13]

What are voice prostheses and heat and moisture exchangers?

A voice prosthesis is a small medical device that incorporates a one-way valve, allowing patients to produce sounds by directing air from their lungs, through the valve, and into their mouth. Typically, the voice prosthesis is placed in a surgically created fistula in the tracheoesophageal wall. Speakers can move air from the trachea through the pharyngoesophageal segment either by manually obstructing the stoma or by using a laryngectomy speaking valve. Subsequently, the movement of oral cavity structures shapes the sound into words for speech production.[13]

Voice prostheses (VP) can be classified as either indwelling or non-indwelling based on whether they can be removed and managed by the patient. Non-indwelling prostheses are removable by patients and can be changed, yet this requires the stoma to be easily accessible and for patients to have sufficient eyesight and dexterity to remove and reinsert the device.[20] Indwelling prostheses are exclusively changed by healthcare professionals (e.g., physician or speech-language pathologist) and often have a longer lifespan than non-indwelling prostheses.[13,20] Device life or durability significantly impacts patient satisfaction and quality of life.[21] The median device life before leakage was generally longer for indwelling prostheses (70 days) compared to non-indwelling prostheses (38 days).[21] On average, TEV speakers require 4 to 6 VP replacements annually, making management and replacement potentially costly.[13]

Ensuring sufficient heat and moisture to the airway, often using heat and moisture exchangers, or alternatively an external humidification system, is also important as the disconnection of the upper and lower airways results in the loss of natural conditioning of inhaled air (humidification, filtration, and heating).[10-12] Heat and moisture exchanger (HME) devices were introduced for patients following total laryngectomy in the 1990s.[10] These devices help compensate for the loss of the upper airway's natural humidifying and filtering functions after laryngectomy. Although some studies have shown that HMEs could potentially improve pulmonary function, reduce respiratory symptoms, and enhance overall quality of life compared with the conventional external humidification system, these potential benefits are limited in the short term (e.g., within approximately 12 days or 6 weeks) and are not consistently observed across all clinical outcomes.[11,12] It is important to note that voice prostheses and HMEs can be used independently, and patients who use an electrolarynx following a total laryngectomy can still benefit from HMEs for pulmonary rehabilitation.[22]

Why is it important to do this review?

This report was conducted in response to a request from a provincial payer seeking to identify the evidence regarding the effectiveness, costs, and any evidence-based recommendations on the use of these devices for adults following total laryngectomy.

Given the impact on quality of life a total laryngectomy has for patients, it is important to evaluate the clinical- and cost-effectiveness of these devices to inform decision-making. Earlier reviews have noted that the evidence to inform care for post-laryngectomy voice rehabilitation is limited. For instance, a previous rapid review by CADTH published in 2017 indicated that studies of the effectiveness and lifespan of different indwelling voice prostheses for adults following laryngectomy had inconsistent results, and, did not identify any cost-effectiveness studies or clinical practice guidelines.[20] Expenses may be a barrier to patients accessing the devices they need, this issue deserves to be explored.

Objective

This rapid review aimed to collate evidence regarding the clinical and cost-effectiveness of voice prostheses (indwelling and non-indwelling devices) and HMEs for adults following total laryngectomy. This rapid review also summarizes the related guideline recommendations available for this patient population. To contextualize the clinical and economic evidence, this rapid review incorporates the perspectives and experiences of patient partners. The research questions and the inclusion and exclusion criteria (scope of the review) are outlined in the sections below.

Research Questions

1. What is the clinical effectiveness of voice prostheses versus no voice prostheses for adults following total laryngectomy?
2. What is the comparative clinical effectiveness of various indwelling and non-indwelling voice prostheses for adults following total laryngectomy, specifically comparing: indwelling versus indwelling devices, non-indwelling versus non-indwelling devices, and indwelling versus non-indwelling devices?
3. What is the clinical effectiveness of heat and moisture exchangers compared to no heat and moisture exchanger for adults following total laryngectomy?
4. What is the cost-effectiveness of voice prostheses versus no voice prostheses for adults following total laryngectomy?
5. What is the comparative cost-effectiveness of various indwelling and non-indwelling voice prostheses for adults following total laryngectomy, specifically comparing: indwelling versus indwelling devices, non-indwelling versus non-indwelling devices, and indwelling versus non-indwelling devices?
6. What is the cost-effectiveness of heat and moisture exchangers compared to no heat and moisture exchanger for adults following total laryngectomy?
7. What are the evidence-based guidelines regarding the use of voice prostheses or heat and moisture exchangers for adults following total laryngectomy?

Methods

An information specialist conducted a customized literature search, of databases and grey literature on July 18, 2024. This search was updated November 19, 2024. One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1. One reviewer extracted data from the included studies and completed critical appraisals.

No changes to the report objectives or research questions or literature search strategy were made to this updated review. The updated rapid review has been augmented to incorporate independent clinical review from an experienced speech and language pathologist and lived experiences from 3 laryngectomee patient partners (inputs gathered via 1 written input and 2 semi-structured interviews).

Appendix 1 presents a detailed description of methods along with the Search Strategy.

Table 1: Selection Criteria

Criteria	Description
Population	Adults following total laryngectomy
Intervention	Q1,2,4,5,7: Voice prostheses including: • Indwelling types (e.g., (including but not limited to) Provox Vega, Blom-Singer Dual Valve, Provox 2, Blom-Singer Classic) • Non-indwelling prostheses types (e.g., (including but not limited to) Provox NiD, BlomSinger Low Pressure) Q3,6,7: Heat and moisture exchanger, with or without voice prostheses
Comparator	Q1,4: No voice prostheses (i.e., esophageal voice) Q2,5: Compared to indwelling or non-indwelling voice prosthesis types, inclusive of the following comparisons: • Indwelling versus indwelling voice prostheses • Non-indwelling versus non-indwelling voice prostheses • Indwelling versus non-indwelling voice prostheses Q3,6: No heat and moisture exchanger Q7: NA
Outcomes	Q1-3: Clinical benefits and harms (e.g., quality of life, patient satisfaction, depression, anxiety, self-esteem changes, device lifespan, safety) Q4-6: Cost-effectiveness (e.g., cost per QALY gained, ICER) Q7: Recommendations regarding the use of voice prostheses (indwelling or non-indwelling) and heat moisture exchangers
Study designs	Health technology assessments, systematic reviews, primary clinical studies, economic evaluations, evidence-based guidelines For Q1-3, we prioritized evidence from systematic reviews over primary studies, as available. Primary studies contained within included systematic reviews and reporting data for the same comparison-outcome were excluded. Single-arm studies were excluded.
Exclusion Criteria	Articles focused on alternatives to voice prostheses (e.g., electrolarynx)
Publication characteristics	English-language reports since January 1, 2019. Systematic reviews published since 2019 were eligible, including those that searched primary studies from database inception, capturing literature published prior to 2019.

ICER = incremental cost-effectiveness ratio; NA = not applicable; Q = research question; QALY = quality-adjusted life-year

Findings

We identified 9 publications eligible for inclusion including 5 systematic reviews,[24-28] 3 economic evaluations,[29-31] and 1 evidence-based guideline.[32] Figure 1 (Appendix 1) presents the PRISMA[33] flowchart of the study selection. Appendix 2 presents additional characteristics of the included studies. This is a relatively small patient population which inhibits traditional approaches and highest standards of methodology in primary research. Owing to various methodological limitations, confidence in the evidence identified was assessed as very low. Appendix 3 provides additional details regarding the strengths and limitations of included publications.

Appendix 4 presents results by different outcomes and clinical questions. Appendix 5 presents to the GRIPP2 (SF) table, and, Appendix 6 presents the list of excluded studies.

Patient profiles

We engaged with 3 patients who have had a laryngectomy. All patients interviewed were patients who had been fitted with a VP and use HMEs. 2 patients use an indwelling VP device and 1 uses a non- indwelling VP device as they require the ability to replace the device themselves due to living far from the hospital. All patients use heat and moisture exchangers on a daily basis. Two of the patients interviewed were female and the other male, all are now retired and all currently live in British Columbia, with one being initially diagnosed and treated in Ontario. The 3 patients interviewed are 1 year, 7 years, and 10 years, post-laryngectomy.

Research Question 1: The clinical effectiveness of voice prostheses versus no voice prostheses for adults following total laryngectomy

2 systematic reviews assessed the impact of TEV using VPs on quality of life compared to EV without using VPs.[24,28]

One systematic review (Maniaci 2024) examined 15 observational studies (11 retrospective controlled studies and 4 uncontrolled retrospective studies) involving 1,085 patients who had undergone total laryngectomy for advanced laryngeal cancer. Most of the participants were male (89.38%), with a mean age of 65.38 years. The intervention group (TEV) consisted of 869 patients who received voice prosthesis rehabilitation (80.1%), while 216 patients (19.9%) were treated with EV. The clinical outcomes assessed included the Voice Handicap Index (VHI), Voice-Related Quality of Life (VRQOL), and the 36-Item short form survey instrument (SF-36). Our patient partners stated that VPs are helpful for communicating with others and are important for their physical, mental, and emotional well-being, which closely relates to these quality-of-life measures.

The second systematic review (Plotas 2024)[28] included 9 observational studies. The sample size of participants with total laryngectomy ranged from 18 to 133, with all participants being 45 years or older.[28] This review (Plotas 2024) evaluated the impact of esophageal voice on various quality of life measures, such as the VHI, VRQOL, and the SF-36, comparing it to baseline measures or other voice restoration methods (e.g., TEV). The systematic review (Plotas2024) presented data at the individual study level but did not perform meta-analyses to pool the results.[28] This systematic review found that patients who received voice rehabilitation with either TEV or EV had significant improvements in their quality of life and communication compared to those who did not.[28]

The details of the outcome measures (e.g., score range and minimal important difference), duration of disease, details on radiotherapy, and the length of follow-up were not reported for both systematic reviews (Maniaci 2024 and Plotas 2024).[24,28]

VHI (2 systematic reviews)

2 systematic reviews evaluated the effectiveness of TEV compared to EV in improving VHI

- In one systematic review (Maniaci 2024, 9 studies), the TEV group demonstrated a statistically significant improvement in VHI compared to the EV group based on the mean scores.[24] Details of the statistical analysis methods were not reported.
- In one systematic review (Maniaci 2024, 5 studies), the meta-analysis using random-effect models indicated that the mean differences in VHI between the two groups was not statistically significant.[24] The 95% confidence interval was wide and included the potential that either of the treatments compared could be favoured.
- In a second systematic review (Plotas 2024, the number of studies contributing to the outcome was unclear), the authors indicated that TEV may perform better than EV in VHI scores, according to a summary of individual studies.[28]

VRQOL (2 systematic reviews)

2 systematic reviews evaluated the effectiveness of TEV compared to EV in improving VRQOL.

- In one systematic review (Maniaci 2024, 7 studies), the TEV group showed a non-statistically significant difference compared to the EV group based on the mean scores.[24] Details of the statistical analysis methods were not reported.

- In one systematic review (Maniaci 2024, 3 studies), the meta-analysis using random-effect models also indicated that the mean differences between the two groups was not statistically significant.[24]
- In a second systematic review (Plotas 2024, the number of studies contributing to the outcome was unclear), the authors indicated that TEV may perform better than EV in VRQOL scores, according to a summary of individual studies.[28]

SF-36 (2 systematic reviews)

2 systematic reviews[24] evaluated the effectiveness of TEV compared to EV in improving SF-36 scores.

- In one systematic review (Maniaci 2024, 4 studies), the TEV group demonstrated a statistically significant better improvement in SF-36 compared to the EV group based on the mean scores.[24] Details of the statistical analysis methods were not reported.
- In one systematic review (Maniaci 2024, 4 studies), no meta-analysis was performed for SF-36.[24]
- In the second systematic review (Plotas 2024, the number of studies contributing to the outcome was unclear), the authors indicated that TEV may perform better than EV in SF-36 scores, according to a summary of individual studies.[28]

The two overlapping systematic reviews (Maniaci 2024 and Plotas 2024)[24,28] present differing conclusions about the comparative effects, highlighting inconsistency in findings. The 2 systematic reviews included some of the same studies, although they used the data from these studies differently and presented different summaries relevant to the research question.

Both systematic reviews had critical flaws leading to critically low confidence in their results. For both reviews, the objective was clearly described, keywords of the search strategies were provided, and study selection processes were reported. Searches were conducted in multiple databases. No systematic review provided the list of excluded studies which prevented assessing whether any relevant studies had been inappropriately excluded. It was unclear how article selection and data extraction were conducted. The possibility of inappropriate inclusion or exclusion or errors in data extraction cannot be ruled out. Risk of bias for included studies was conducted yet the reviews did not explore the potential impact of risk of bias on result interpretations. Plotas 2024[28] reported excluding studies with high RoB in the method section, but it noted that most of included studies in this review had weak methodologies and high bias in their result section. Maniaci 2024[24] reported that most of the studies had low RoB and assessed the quality of evidence using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework, the details of the GRADE assessment were unclear and did not adhere completely to the GRADE principles as it started the certainty of evidence at very low for evidence from observational studies and did not assess the certainty of evidence for each outcome. The accuracy of the overall certainty of evidence appraisals was uncertain and difficult to interpret in this review.

Research Question 2: The clinical effectiveness of indwelling and non-indwelling voice prostheses for adults following total laryngectomy, specifically comparing: indwelling versus indwelling devices, non-indwelling versus non-indwelling devices, and indwelling versus non-indwelling devices

2 systematic reviews comparing the effectiveness of different voice protheses on clinical outcomes were identified (Mayo-Yanez 2023 and Tawfik 2021)[26,27].

1 systematic review (Mayo-Yanez 2023)[26] included 4 observational studies involving 55 laryngectomy patients (87.27% male, mean age 62.71 years) who used VP. The studies compared the Provox Vega XtraSeal (PVX) prosthesis (n=94) to control VPs (Vega and ActiValve Light, n=221) and focused on VP duration.

1 systematic review (Tawfik 2021) with network meta-analysis (NMA)[27] included 120 studies with 11,918 laryngectomy patients (71.7% male, aged 17 to 90 years). The analysis evaluated 10 VPs including 8 indwelling prostheses [Provox-1, Provox-2, Provox ActiValve, Provox Vega, Sound-Producing Voice Prosthesis (SPVP), Nijdam, Groningen Low Resistance, Groningen Ultra Low Resistance] and 2 non-indwelling prosthesis [Provox non-indwelling device (NID) and Blow-Singer low pressure (BS-LP)] on multiple clinical outcomes, such as VP replacement, VP duration, airflow resistance, leakage rates, and patient device preference, with follow-up durations ranging from 0.5 to 133 months (about 11 years). This systematic review (Tawfik 2021) also evaluated use of HMEs in the NMA and compared different VPs to HMEs for some outcomes.[27] This systematic review did not clarify whether the VP arm included patients with or without a HME.[27] The results related to the comparisons of HMEs were not included in this report.

Comparisons among 10 VPs (8 indwelling and 2 non-indwelling)

1 systematic review (201 studies) and NMA (120 studies) [27] compared the effectiveness of 10 VPs (8 indwelling and 2 non-indwelling devices): Provox-1, Provox-2, Provox AV, Provox Vega, SPVP, Nijdam, Groningen Low Resistance, Groningen Ultra Low Resistance, Provox NID, and BS-LP. For most comparisons, across most clinical outcomes, the NMA was insufficient to show a difference between the devices being compared.[27] Many effect estimates were imprecise. The 95% CIs were wide, including the potential that either treatment being compared could be favoured.

Provox VegaTM XtraSealTM (PVX) compared to control VP (Vega and ActiValve Light)

1 systematic review (Mayo-Yanez 2023, 4 studies)[26] compared the lifespan of PVX and control voice prostheses (Vega and ActiValve Light) and reported that PVX had a numerically longer mean lifespan than the control VPs. However, the review (Mayo-Yanez 2023) did not perform statistical tests to compare the two groups, and the 95% confidence intervals overlapped.

Both systematic reviews had critical flaws, leading to critically low confidence in their results. The review objectives were clearly described, keywords of the search strategies were provided, and study selection processes were described. Both systematic reviews conducted their searches in multiple databases. 1 systematic review reported performing a grey literature search.[27] Neither provided the list of excluded studies. These limitations may result in missing some eligible studies. At least 2 reviewers independently performed or verified the article selection and data extraction in 1 systematic review.[25,27] Two reviewers independently conducted data extraction in 1 systematic review (Mayo-Yanez 2023), but it was unclear how the article selection was performed.[26] The possibility of inappropriate inclusion or exclusion or errors in data extraction cannot be ruled out.

1 systematic review (Mayo-Yanez 2023) assessed the risk of bias of included individual studies and reported study quality yet did not provide an overall summary of the risk of bias (RoB). Neither review explored the potential impact of risk of bias on result interpretations. Tawfik (2021)[27] stated that all 32 included RCTs had either low (n=9) or unclear (n=23) RoB. However, this review (Tawfik (2021) also included approximately 169 observational studies, of which 32 were ranked as good, 107 as fair, and 30 as poor.[27] The findings of some of these systematic reviews may be driven by studies with high risk of bias.

Tawfik 2021[27] conducted a frequentist network meta-analysis (NMA) comparing 10 VPs: Provox-1, Provox-2, Provox AV, Provox Vega, SPVP, Nijdam, Groningen Low Resistance, Groningen Ultra Low Resistance, Provox NID, and BS-LP. The NMA presented a range of results, including network plots, point estimates, 95% confidence intervals, and p-scores. Intervention rankings were based solely on p-scores without considering the results of statistical tests or the certainty of the evidence. This approach means that VPs with top rankings may have low-certainty evidence or may not show statistically significant differences compared to other VPs. The systematic review (Tawfik 2021) noted some variability, or heterogeneity, among the included studies. However, it did not adequately assess potential treatment effect modifiers or how these factors could influence the assumption of exchangeability. This may introduce bias into the results of the NMA due to the insufficient evaluation of the validity of the exchangeability assumption. Additionally, the inclusion of non-randomized studies in the NMA could have introduced bias due to the inherent limitations of observational studies, such as selection bias and confounding factors. We also compared the registered systematic review protocol in PROSPERO (CRD42017080110) with the published reviews and identified several discrepancies. For instance, the protocol specified the inclusion of only RCTs, but the published review also included observational studies. Additionally, while the protocol focused solely on VPs, the review incorporated the HME devices in the NMA for certain outcomes, such as patient preference. The authors did not address these deviations between the review protocol and their actual work. In addition, a commentary on this review raised concerns about the accuracy and completeness of the findings, citing errors in data extraction, the exclusion of relevant studies, and the absence of crucial clinical outcomes, such as quality of life.[34]

Research Question 3: The clinical effectiveness of heat and moisture exchanger for adults following total laryngectomy

1 systematic review (Ahmed 2023, 10 studies)[25] evaluated the effectiveness of HMEs compared to non-HME or EH on various outcomes.

This review (Ahmed 2023) identified 1 mixed-methods study[25] that included a rapid review, which met our criteria for systematic review for the purpose of rapid response, we refer to the rapid review as a systematic review in our report. The review (Ahmed 2023) compared the effectiveness of HMEs with no HME use or external humidifier. The review (Ahmed 2023) included 10 studies

comprising 3 RCTs, 3 time-series studies, 2 retrospective studies, 1 case-control study, and 1 study with an unclear design. The review (Ahmed 2023) included 550 patients who underwent total laryngectomy. Age and sex data were not reported. The intervention involved the use of HMEs, compared to baseline, no HME use, an external humidifier or another HME. This report only summarized the comparisons between HMEs compared to no HME or external humidifier use. The review (Ahmed 2023) summarized several clinical outcomes including mucus production, coughing, forced expectorations, the number of days requiring chest physiotherapy after surgery, tracheobronchitis or pneumonia episodes, patient satisfaction, quality of life, sleep quality, speech quality, and social contacts. The follow-up duration for these outcomes was either 3 months or not reported.

HMEs were reported to statistically reduce various outcomes[25]: mucus production, coughing, forced expectorations, the number of days requiring chest physiotherapy after surgery, tracheobronchitis or pneumonia episodes. HMEs were reported to statistically improve patient satisfaction.[25] The difference between HME and control (non-HME or external humidifier) are not statistically significant in the following outcomes:[25] QOL, Sleep Quality, Speech Quality, Social contacts.

This review had multiple critical flaws, leading to critically low confidence in results. The objective was clearly described, keywords of the search strategies were provided, and study selection processes were described. PubMed was searched and no grey literature search was reported, the review did not provide the list of excluded studies which may result in missing some eligible studies. 2 reviewers independently performed or verified the article selection and data extraction. This review did not assess the risk of bias of included studies.[25]

Summary of patient experience using VPs and HMEs

The following section provides an overview of the patient experience collected from 3 patient partners. This section reports examples of individual experiences in using VPs and HMEs. Head-to-head comparisons of VPs and HMEs is outside of the scope of this rapid review. Given the small sample of interviewed patients, these reported examples are not indicative of device superiority.

All 3 patient partners engaged in this project use different models of voice prothesis and heat moisture exchangers and described trying and using different device models to find those that best aligned with their needs and preferences. Patients emphasized selecting device models that could best accommodate their physical comfort and needs (e.g., limited leakage), costs, geographical residence, and unique circumstances, such as physical changes due to radiation therapy, wildfire smoke, special occasions, and when susceptible to airborne pathogen exposure. For example, 1 patient used the indwelling Atos brand Provox VP after trying the Blom-Singer prosthesis, because it best suited them and did not cause inner barrel leakage. Another patient found that the Provox Tru-Tone Emote electro-larynx allowed patients to speak after radiation therapy while being cheaper than the previously used Provox Vega 17Fr VP. Another patient used a non-indwelling VP (Provox NiD), which they changed themselves to avoid travelling over 3.5 hours to reach the hospital. This patient described travelling long distances to change the device as impractical, noting that other updated models need to be changed by the Speech and Language Pathologist (SLP). Patients also used different HME models. They reported using Atos Extra flow and Provox ExtraMoist, switching to other HME models in unique circumstances, such as Hands-free HME from Inhealth Technologies on ‘special occasions,’ Provox Micron HME when the wildfire smoke was bad, or in situations with a high risk of airborne pathogen exposure. One patient reported that an SLP demonstrated EV, but the patient did not describe detailed personal experiences with it. The patient mentioned TEV was easier to learn than EV, and they never encountered one who used EV exclusively.

Patients reported 3 benefits from using their VPs and HMEs, including improved communication, independence, and infection control. Patients described being able to live life and communicate with family and friends as the most important benefit. The patients talked about the isolation and frustration when they were unable to communicate and when using ‘Type to Speak’ Apps, which caused breaks in conversation and missed opportunities to communicate. Having a VP and HME allowed patients to be independent – allowing them to communicate in person and on the phone. They mentioned being independent to be important for their physical, mental, and emotional wellbeing. Whilst the VP allows the patient to communicate, which some patients commented was a basic human right, it was also felt that the HMEs were vital in saving their lives from infection.

Patients described 3 challenges with using their VPs and HMEs, including device limitations, environmental impact on use (i.e., the weather and wildfires), and maintenance. Device limitations included several considerations such as the impossibility of changing the volume of the VP, making it difficult to communicate in loud or quiet places, and not being able to change the pitch of the voice,

with 1 patient emphasizing that their voice no longer sounded like themselves. However, they noted that being able to communicate far outweighed these limitations. Patients noted the ability to communicate and engage with others in public was limited; they reflected that the need to obscure their stoma to talk meant they needed to avoid touching others (i.e., shaking hands) or touching surfaces to help prevent any potential infection. One patient mentioned being allergic to the adhesive on the hands-free HME, wearing a HME that they had to occlude themselves. Another patient mentioned that the softer silicone design of the 1 VP device (Blom-Singer prosthesis) caused their fistula to distort out of shape, causing inner barrel leakage. Additionally, talking while eating or drinking was not possible as the food or liquid may have inadvertently got into the lungs – and some patients commented that they often drink privately to avoid leakage through their stoma.

Patients reported that the weather had a significant impact on being able to effectively use a VP and HME. The cold air can be painful, cause irritation, and cause the lungs to fill with liquid. One patient mentioned that the negative impact of cold weather was a large driving factor for moving to a different province with warmer annual temperatures. The hot air can be an irritant as well, and the moist air can cause coughing resulting in pain. Wildfires create additional challenges, with the HMEs getting frequently blocked and needing to use more or different devices to prevent infection.

Device maintenance was another challenge. Changing the VP can be a problem especially when living far from the hospital. One patient living 3.5 hours from the nearest hospital chose a non-indwelling VP that she could change herself. However, this device choice caused problems with leakage when drinking and led her to drink in the bathroom. Keeping the devices clean can also be a challenge. patients mentioned needing to clean the VP between once every other day to as much as 4 times per day due to food build up. Patients also mentioned about needing to replace their device as frequently as every 5 weeks for one patient and on average 3 times per year for another. This issue changed their eating habits and limited their eating. Patients noted that having a VP that needs to be replaced by the specialist meant that replacing the VP in case of a problem became an emergency – “you need to order yourself and then travel to the appointment and hope the new device fits.” Patients mentioned that when they went out, they needed to take a bag of supplies with them to help them maintain their device or manage any challenges, i.e., additional HMEs, adhesive tape, tissues etc. They also noted that sneezing and coughing can cause a large amount of mucus to get stuck in the HME and therefore have to throw it away, patients commented on having to try to remove the device before coughing and sneezing.

Research Question 4: The cost-effectiveness of voice prostheses versus no voice prostheses for adults following total laryngectomy

No eligible studies were identified.

Research Question 5: The cost-effectiveness of indwelling and non-indwelling voice prostheses for adults following total laryngectomy, specifically comparing: indwelling versus indwelling devices, non-indwelling versus non-indwelling devices, and indwelling versus non-indwelling devices

No evidence was found comparing the cost-effectiveness of indwelling versus non-indwelling voice prostheses, nor between different non-indwelling VPs for adults following laryngectomy.

2 cost-effectiveness studies[29,30] that compared a regular indwelling VP (Provox Vega®) and its modified versions designed to prevent leakage (Provox XtraSeal® and Provox ActiValve®) were identified.

1 study (Rodriguez-Lorenzana 2023)[29] compared the cost-effectiveness of Provox Vega® against the Provox XtraSeal®. The study used data on 551 VPs (483 Provox Vega®, 68 Provox XtraSeal®) from 38 patients (35 men, 3 women) with a mean age of 66 from 2015 to 2023.[29] The incremental cost-effectiveness ratio (ICER) was calculated from the Spanish National Health System's perspective, based on the difference in costs and the number of annual prosthesis replacements.[29]

1 study (Mayo-Yanez 2022)[30] compared the Provox Vega® to the Provox ActiValve®, which features a magnet-based valve to prevent leakage. The study included 159 VPs (150 Provox Vega®, 9 Provox ActiValve®) from 5 Caucasian men with a mean age of 64.[30] The ICER was calculated based on the number of annual prosthesis replacements during the observational study from the perspective of the Spanish Public National Health System.[30]

Reported results comparing a regular indwelling VP (Provox Vega®) and its modified versions for laryngectomized patients experiencing leakage with Provox Vega based on Spanish National Health System perspective:[29,30]

- Switching to Provox XtraSeal is cost-effective if the cost of Provox XtraSeal remains below EUR 551.63.[29]
    - ICER (EUR/Effectiveness): -0.01
        - Lower cost scenario: EUR -291.80
        - Higher cost scenario: EUR 93.07
- Switching to Provox ActiValve is also cost-effective:[30]
    - ICER (EUR/Effectiveness): -133.97

Both studies clearly defined their research questions, study design, data collection parameters, outcome measures, analysis perspectives, and rationale for selecting the study alternatives. The rationale for the chosen form of economic analysis could have been further elaborated. Each study's effectiveness measures were derived from a single prospective study with small patient samples (5 or 38 VP users, 40 HME users, 22 ASC users). Both studies[29,30] focused on the cost-effectiveness of different indwelling VPs based on cross-over studies. These studies involved Provox Vega users who experienced 3 or more consecutive changes due to leakage, which affected the prosthesis's theoretical lifespan. The patients then switched from the Provox Vega to its alternatives (Provox XtraSeal or Provox ActiValve). This transition introduced variability in the background care, or surgical interventions received, making comparisons between the devices less consistent. Both studies[29,30] also lacked details on currency adjustments for inflation or conversion and did not include sensitivity analyses. These studies[29,30] were conducted from the payer's perspective within the Spanish National Health System, their findings may not be applicable to the Canadian healthcare system.

Research Question 6: the cost-effectiveness of heat and moisture exchanger for adults following total laryngectomy

This review included 1 study[31] that compared cost-effectiveness of HMEs versus alternative stoma covers (ASC) in post-laryngectomy patients at a clinic in Massachusetts, USA. The study (Beck 2020), conducted from September to December 2018, included 40 HME users and 22 ASC users, mostly male (71%).[31] Quality of life (QoL) data were collected via a study specific questionnaire and the utility index scores were derived using the EQ-5D and the US tariff.[31] A Markov model calculated the ICER by dividing the total cost difference by the difference in quality-adjusted life years (QALYs) from a US healthcare and societal perspective.[31]

This review included 1 study[31] that compared cost-effectiveness of HMEs versus ASCs in post-laryngectomy patients from the US healthcare and societal perspective. The study found that HME use is cost-effective compared to ASCs:[31]

- QALYs were slightly higher for HME users compared to ASCs
- Total lifetime costs per patients were higher for ASCs users compared to HME users
- ICER (US $/QALY): healthcare perspective: -11,833; societal perspective: -306,551
- Annual budget saving (US $): healthcare perspective: 1,551,083; societal perspective: 40,183,593

The study clearly defined their research questions, study design, data collection parameters, outcome measures, analysis perspectives, and rationale for selecting the study alternatives. This study provided a comprehensive economic evaluation, justifying its choice of economic model, clearly defining effectiveness estimates and outcome measures, and including appropriate sensitivity analyses. This study was conducted from both a U.S. healthcare and societal perspectives and findings may not be generalizable to the Canadian context due to differences in healthcare systems.

Summary of Patient Experiences related to device costs

Costs associated with device use were reported as a significant challenge for all 3 patients interviewed. Patients reported being impacted by the cost of the VP and HME devices, and, also the cost of maintenance items, such as medical tape, tissues, infection

prevention cream, and cleaning materials. Patients mentioned that there was varying coverage for the costs of the VP, HMEs and associated supplies, across the country. For example, in British Columbia, where all engaged patients lived, there is currently no funding for supplies, and this was seen as the biggest frustration from patients. One patient previously lived in Ontario, noting that in that province there was some financial funding to support the purchase of supplies for patients with laryngectomy. Some patients mentioned those on lower incomes would struggle to afford VP, HMEs and additional supplies needed to appropriately manage and maintain the device.

High costs for the VP and the HMEs, which need to be changed often—patients commented on needing to change 3-4 times per year in addition to the HMEs—the latter needing to be replaced daily or more if cough/sneeze or air quality was bad.

All 3 patients used an HME; however, due to the cost of these, they tried to minimize the use in the home. Sneezing and coughing can cause a large amount of mucus to get stuck in the HME and therefore needs to be thrown away. Patients commented on having to try to remove the HME before coughing and sneezing, with 1 patient referring to this as a "$5 sneeze." One patient, very generously, provided a breakdown of the personal expenses for yearly maintenance of his laryngectomy totaling **$7844 per year**. Specifically: Voice prosthesis 3/yr- $1540.00, HME - $1656.00, Adhesive patches - $2640.00, Foam patches - $168.00, Liquid calcium - $832.00, Atos cleaning brushes - $480.00, Hydrogen peroxide - $96.00, Polysporin cream - $192.00, Tissues - $240.00.

Research Question 7: the evidence-based guidelines regarding the use of voice prostheses or heat and moisture exchanger for adults following total laryngectomy

1 evidence-based guideline that provided recommendations regarding the use of voice prostheses for adults following laryngectomy in managing periprosthetic leakage was identified.[32] No evidence-based guideline regarding the use of HME for adults following laryngectomy was identified; therefore, no summary can be provided.

The guideline was developed in Spain aimed at healthcare professionals, including otorhinolaryngology specialists, speech therapists, nursing staff, and other specialists, with a focus on laryngectomized patients.[32] The evidence was collected and synthesized through a systematic review of 91 studies on primary or secondary TEP (which does not address the same research questions as the current report), assessed using the Oxford Levels of Evidence system (2011), ranging from level 1a (systematic reviews of RCTs) to level 5 (mechanism-based reasoning). The guideline development group reviewed recent research on benefits, side effects, and risks to make recommendations with a grade of recommendation (B or C), however, the meaning of these recommendation grades was not specified.[32]

The guideline recommended replacing the prosthesis with a double-flanged one, such as PVX, or adjusting the diameter and length, or placing a silicone sheet (or ring) on the tracheal side of the prosthesis. It also mentioned that the Blom-Singer large esophageal and tracheal flange VP is a useful solution for managing periprosthetic leakage. However, the guideline did not provide clear recommendations regarding the initial use of VPs.

The included evidence-based guideline had clear objectives, guideline questions, and target populations (e.g., patients undergoing total laryngectomy).[32] The guideline development group searched multiple databases (MEDLINE, Embase, Scopus, Web of Science, PubMed, Science Citation Index, and The Cochrane Library) for relevant evidence and then achieved consensus to formulate recommendations.[32] The guideline panel included otolaryngologists, head and neck surgeons, and expert speech therapists.[32] However, it is uncertain whether at least one methodology expert was involved in the development of the guideline and whether the perspectives or preferences of the target populations were sought or had an influence on the recommendations. Therefore, the recommendations may not adequately reflect the values and preferences of patients or other partners.

The guideline[32] proposed using either B or C for the grade of recommendations; the meaning of recommendation grades was not specified, limiting the interpretation of the recommendations. The links between the recommendations and the supporting evidence were unclear. The guideline was funded by Atos Medical and all guideline authors disclosed no competing interests. The included guideline discussed the potential facilitators to implementing some recommendations and considered some cost-effective evidence.[32] The guideline did not discuss the related barriers regarding the use of VP, such as accessibility and affordability for the VP, which could be a barrier to implementing related recommendations.

Limitations

Our rapid review has several limitations. The patient engagement component included 3 patient partners, all of whom were residents of British Columbia, with 1 having relocated from Ontario. Feedback obtained during these engagement activities revealed potential jurisdictional variations in coverage policies for VPs, HMEs, and related supplies. The findings engagement with patients may not be fully representative of the broader spectrum of patient perspectives across Canada. Furthermore, the patient engagement activities did not yield information regarding patient experiences with esophageal voice; therefore, a comparison between the experiences of vocal prosthesis users and those using esophageal voice remains unexplored.

Patient and clinician engagement occurred after the first version of this rapid review was complete and did not influence the formulation of research questions or outcomes of interest, which may limit the relevance and applicability of the findings. Research questions addressed only a subset of this broader clinical topic regarding care for adults following total laryngectomy, potentially overlooking important factors such as patient values, preferences, and accessibility. Our rapid review did not directly compare different types of head and neck management techniques or investigate other critical comparisons (e.g., TEV versus electrolarynx), which affects its comprehensiveness and utility for decision-making. Our search is limited to the past five years, despite the search dates for the included literature dating back to the 1980s, it is possible that some relevant literature has not been identified.

Our report relies on systematic reviews; however, our confidence in their results was very low, making them unreliable for providing an accurate and comprehensive summary of the available evidence. Two systematic reviews (Maniaci 2024 and Plotas 2024) included overlapping individual primary studies, which may lead to potential aggregate biases. Although this report included 5 systematic reviews[24-28] addressing the clinical effectiveness of VPs compared to no VPs or another alternative VP and considering many primary studies, due to various methodological flaws, again, our confidence in the results of these reviews is very low. These systematic reviews also did not directly address the same research questions as the current report. As such, these reviews should not be relied on to provide an accurate and comprehensive summary of the available studies answering the research questions.

The body of evidence identified suffers from substandard reporting. None of the included systematic reviews focus on adverse outcomes associated with different voice restoration methods. The details of the QoL outcome measures (e.g., score range and minimal important difference) and the length of follow-up were not reported.[24,28] This review identified evidence gaps as no high-quality systematic reviews that directly address our research questions were available. We base our conclusions on statistical significance, it is important to note that statistically significant results may lack practical clinical importance, and non-significant results do not necessarily indicate no difference. In some systematic reviews, the effect estimates were challenging to interpret due to non-reporting of outcome definitions, the range and direction of scores on measurement scales, and units of measurement.

We did not limit VP or HME devices by product, as such, some of the devices detailed in identified systematic reviews may not be available in Canada. The included economic evaluation studies were conducted from the perspectives of the US and Spanish National Health System.[29-31] No evidence-based guidelines or economic evaluations were identified focused on the Canadian context. The included guidelines were conducted in Spain,[32] and no guideline authors were from Canadian institutions, as such, the generalizability of the findings to settings in Canada is unclear.

Conclusions and Implications for Decision- or Policy-Making

This rapid review summarizes evidence on the effectiveness and cost-effectiveness of VPs and HMEs compared to no VP and, or HME for adults following total laryngectomy. According to feedback from clinicians, use of voice protheses and heat and moisture exchangers following total laryngectomy are reported to have been common clinical practice in Canada for many years. The impact of total laryngectomy on patients' quality of life is significant. Both the literature, and our interviews with 3 patients revealed that VPs and HMEs significantly benefit post-laryngectomy quality of life, primarily by restoring communication and social engagement. HMEs are reported as necessary for infection prevention. While these devices are reported to enhance independence, social engagement, and overall quality of life, there are reported challenges with use, including device limitations (e.g., fixed volume/pitch, inability to speak and drink simultaneously), environmental sensitivities to extreme temperatures or forest fire smoke, and the need for frequent maintenance (VP replacements 2-3 times per year, daily HME changes). Out-of-pocket costs related to the use of VPs, HMEs, and related supplies were reported to present a major barrier for patients, causing significant financial strain and frustration.

Potential inequities were observed. For example, rural or remote locations may impact a patient's choice of device as some VPs can only be fitted by SLP, therefore, if a patient lives far from hospital facilities, it becomes challenging when there is a fault with the device or when there is the need to routinely change it. One of the patients interviewed chose a non-indwelling VP device to be able to change themselves and not travel to the hospital. Similarly, a patient's ability to change HME and VP, as needed, requires physical mobility and function to maintain their devices appropriately to ensure effective operation. Patients with co-morbidities may need additional routine access to care.

Five systematic reviews,[25-28] 3 cost-effectiveness studies,[29-31] and 1 evidence-based guideline[32] were identified to answer our research questions. No evidence of cost-effectiveness of voice prostheses versus no prostheses, indwelling versus non-indwelling prostheses, or comparisons among different non-indwelling prostheses for adults following laryngectomy was identified. This is a relatively small patient population, as such, achieving the highest standards of methodology - large randomised controlled trials - in primary research is infeasible. Population size, and primary evidence quality subsequently impacts rapid review quality. Owing to various methodological limitations, confidence in the evidence identified was assessed as very low.

Two systematic reviews, for which we had critically low confidence results, suggest that TEV may positively impact QoL measures compared to EV.[24,28] However, the available meta-analyses found no statistically significant differences between TEV and EV in VHI and VRQOL scores,[24] with wide 95% confidence interval, including the possibility of either intervention being favoured. One systematic review indicated that patients undergoing voice rehabilitation with either EV or TEV experienced significant improvements in their QoL and communication compared to those who did not receive voice restoration.[28] The review highlights the challenges associated with EV, including the need for extensive training and its potential to increase fear and anxiety, and reduce self-confidence and self-esteem, which may impact their effective communication and overall functionality.[28] The limited evidence emphasizes the importance of shared decision-making when selecting between TEV and EV. This process should incorporate patient values, preferences, lifestyle, and cost considerations. People should also consider a range of factors impacting patient well-being, such as learning difficulties and anxieties about technologies.

The effectiveness of one model of VP compared with others requires further investigation due to critically low confidence results from one included systematic review (Tawfik 2021).[27] This suggests decision-making should consider patient-centered factors such as individual values, preferences, lifestyle, cost, and ease of maintenance. Other factors influencing the decision to use a VP or select a specific type include post-operative anatomic status, physical and mental capabilities, level of independent functioning, caregiver support, and patient motivation.[13] Our engaged clinical expert noted that choices between indwelling and non-indwelling voice prostheses are often determined by patient and environmental factors; due to the typically lower cost of non-indwelling VP options are frequently considered more suitable for cognitively intact patients living in remote settings or within provinces where voice prostheses are not covered under health plans. The patient engagement findings support the feedback from the clinical expert.

For total laryngectomy patients experiencing leakage with Provox Vega, it may be reasonable to switch to a modified version to prevent further leakage, such as Provox XtraSeal for periprosthetic leakage or Provox ActiValve or Provox ActiValve for endoprosthesis leakage.[29,30,32] It is important to note that eligible studies included in the review only examined and mentioned the Provox brand for managing VP leakage, the switch from a single-valved to a dual-valved VP is driven by the need to address device malfunction in individual patients rather than a specific brand.[35] Patients could switch among different devices to find the most effective option. Alternatively, clinicians or patients can manage leakage by adjusting the prosthesis's diameter and length or placing a silicone sheet (or ring) on the tracheal side of the prosthesis.[32]

1 systematic review (Ahmed 2023) for which we had critically low confidence in its results[25] suggests the potential benefits of HMEs. This review reports HMEs significantly improve several clinical outcomes, including mucus production, coughing, forced expectorations, the number of days requiring chest physiotherapy after surgery, tracheobronchitis or pneumonia episodes, and patient satisfaction. No difference between HME use and control was observed for QOL, sleep quality, speech quality, and social contacts. HMEs were reported to be cost-effective compared to ASCs from the US perspective.[31]

Future systematic reviews should be planned and conducted in alignment with recognized methodological standards and be transparently reported.[36,37] As the certainty of evidence even from high quality systematic reviews relies in part on the risk of bias of their included studies, future primary studies should also be robustly planned and conducted and transparently reported. For example, due to the size of this population, primary studies using data from laryngectomized patient registries may help answer

these research questions. Future cost-effectiveness analyses should include sensitivity analyses to test the robustness of their findings. Future evidence-based guidelines should conduct comprehensive literature reviews, have diversity in panel composition, and formulate recommendations through established consensus processes that involve patient partners or panel members from Canada to enhance the generalizability of recommendations to the Canadian context.

In conclusion, post-laryngectomy interventions include olfactory, voice, swallowing rehabilitation and addressing the psychosocial aspects of patient recovery. Voice rehabilitation is an important aspect of post-laryngectomy care to restore vocal communication, and options include the use of esophageal voice, an artificial larynx (electrolarynx), and, or, tracheoesophageal voice with voice prothesis. The use of voice protheses and heat and moisture exchangers are highly valued by the clinical and patient community we engaged. The evidence base related to their benefit and cost effectiveness is limited. The perspectives of speech and language pathologists working with patients, and patients with lived experience of these devices, may supplement decision-making by contextualizing the evidence currently available. Decisions regarding the choice of voice prostheses should consider patient's tracheoesophageal puncture (TEP) shape and size, patients' values and preferences, accessibility, affordability, and other factors such as physical and mental capabilities, caregiver support, and patient motivation. Limited evidence aligns with reporting from patients and clinicians that adding heat moisture exchangers could be beneficial in several clinical outcomes, such as mucus reduction, reduced tracheobronchitis or pneumonia episodes, and reported patient satisfaction. Additionally, our patient partners highlighted the importance of HMEs in preventing infection. Policy decisions should take into consideration the limited quantity and quality of the current evidence available for this small population of patients. Geographical considerations, patient-comorbidities, and financial barriers for this population of patients should be carefully considered.

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Appendix 1: Detailed Methods and Selection of Included Studies

Literature Search Methods

The literature search strategy used in this report is an update of one developed for a previous CDA-AMC report.[38] For the current report, an information specialist conducted a literature search on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the International HTA Database, the websites of health technology assessment agencies in Canada and major international HTA agencies, as well as a focused internet search. The search approach was customized to retrieve a limited set of results, balancing comprehensiveness with relevance. The initial search was limited to English-language documents published between January 1, 2019 and July 18, 2024. For the current report, database searches were rerun on November 19, 2024 to capture any articles published or made available since the initial search date. The search of major HTA agencies was also updated to include documents published since July 2024. We provide strategies for MEDLINE below; the search strategies for grey literature are available upon reasonable request.

Clinical Literature Search

Overview
Interface: Ovid
Databases
- MEDLINE All (1946-present)

Date of search: July 18, 2024; updated November 19, 2024
Search filters applied: Guidelines (for supplemental search only)
Limits
- Publication date limit: 2019-present
- Language limit: English-language

Syntax	Description
/	At the end of a phrase, searches the phrase as a subject heading
MeSH	Medical Subject Heading
*****	Before a word, indicates that the marked subject heading is a primary topic; or, after a word, a truncation symbol (wildcard) to retrieve plurals or varying endings
adj#	Requires terms to be adjacent to each other within # number of words (in any order)
.ti	Title
.kf	Keyword heading word
.ab	Abstract
.au	Author name
.co	Collaborators involved in the publication (Embase)
.ca	Corporate or institutional author (PsycInfo)
.pt	Publication type
.dt	Date the citation was added to PubMed (used for records beginning December 15, 2008)
.ez	Date the citation was added to PubMed
.da	Date MeSH terms were added to the citation

Warning

To conduct a comprehensive search, we may have included antiquated, noninclusive, or potentially stigmatizing terms that may have appeared in past and present literature. We recognize and acknowledge the inappropriate and harmful nature of terms that may appear in search strategies and include this warning so the reader can determine how they would like to proceed.

The warning is modified from the University of Michigan Library's guidance, Addressing antiquated, non-standard, exclusionary, and potentially offensive terms in evidence syntheses and systematic searches.

Database Strategy
Note: Lines 23 and 24 of the search strategy were included only in the search update; these lines limit the original search to July 2024 onwards. The original search instead limited the date to 2019 onwards.

1 (heat adj2 moisture adj2 exchanger*).ti,ab.
2 Larynx, Artificial/
3 ((Voice* or laryn*) adj4 (artificial* or prosthe* or replace* or replacing)).ti,ab.
4 ((Voice* or larynx* or vocal* or speech) and (indwelling or in-dwelling)).ti,ab.
5 (Provox* or blom-singer* or blom singer).ti,ab.
6 1 or 2 or 3 or 4 or 5
7 Laryngectomy/ or (laryngectom* or post-laryngectom* or postlaryngectom*).ti,ab.
8 (guideline or practice guideline or consensus development conference or consensus development conference, NIH).pt.
9 (guideline* or standards or consensus* or recommendat*).ti.
10 (practice parameter* or position statement* or policy statement* or CPG or CPGs or best practice*).ti.
11 (care adj2 (path or paths or pathway or pathways or map or maps or plan or plans or standard)).ti.
12 ((critical or clinical or practice) adj2 (path or paths or pathway or pathways or protocol*)).ti.
13 (algorithm* and (pharmacotherap* or chemotherap* or chemotreatment* or therap* or treatment* or intervention*)).ti.
14 (algorithm* and (screening or examination or test or tested or testing or assessment* or diagnosis or diagnoses or diagnosed or diagnosing)).ti.
15 (guideline* or standards or consensus* or recommendat*).au.
16 (guideline* or standards or consensus* or recommendat*).co.
17 (guideline* or standards or consensus* or recommendat*).ca.
18 systematic review.ti,pt,kf,sh. and (practice guideline* or treatment guideline* or clinical guideline* or guideline recommendation*).ti,ab,kf.
19 or/8-18
20 7 and 19
21 6 or 20
22 limit 21 to english language
23 (202407* or 202408* or 202409* or 20241* or 2025*).dt,ez,da.
24 22 and 23

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1. Figure 1 presents the PRISMA[33] flowchart of the study selection.

Exclusion Criteria

We excluded publications that did not meet the selection criteria outlined in Table 1, as well as duplicate publications. Additionally, we also excluded expert opinions or guidelines with unclear methods or recommendations, single-arm primary studies, and primary studies already included in at least one eligible systematic review for the same comparison-outcome.

Definitions of systematic review and evidence-based guideline

A review is considered systematic if it includes the following: a) an objective and/or research question(s); b) indications that evidence was searched for in a systematic way (e.g., information on 1 or more of the following provided: names of databases, search platforms/engines, search date, key words or search strategy), and c) inclusion and exclusion criteria. An evidence-based clinical practice guideline is defined as a systematically developed statement or set of statements to assist practitioner- and patient

decisions about appropriate health care for specific clinical circumstances. A guideline is considered evidence-based if a systematic search of the literature was undertaken and a guideline panel was involved to inform the recommendations.

Critical Appraisal of Included Studies

The included studies were critically appraised by 1 reviewer using the following tools as a guide: A Measurement Tool to Assess systematic Reviews 2 (AMSTAR 2)[39] for systematic reviews and the "Questionnaire to assess the relevance and credibility of a network meta-analysis"[40] for systematic review and network meta-analyses, Drummond checklist[41] for economic evaluations, and the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument[42] for guidelines. Summary scores were not calculated for the included studies; rather, the strengths and limitations of each included publication were described narratively.

Clinical Expert, Public and Patient Engagement Process

This rapid review has been updated to augment findings of the rapid literature review with clinical and patient experience. A clinical reviewer was sourced via Speech-language & Audiology Canada and contracted to provide detailed peer review of the drafted report, specifically to review any potential clinical misunderstandings and to supplement the clinical context for this relatively small population of patients.

Patient Engagement

We included the perspectives of 3 patients with lived experience of using a VP and HMEs after having a laryngectomy.

Invitation to Participate and Consent

We reached out through email directly to patient advocacy groups. The preliminary engagement request included an overview of this project, the purpose of engagement, and the nature of engagement activities. Members of a patient group identified themselves as being interested in sharing their experiences. The CAD-AMC Patient Engagement Officer obtained the person's informed consent to share their lived experiences regarding their VP and HME.

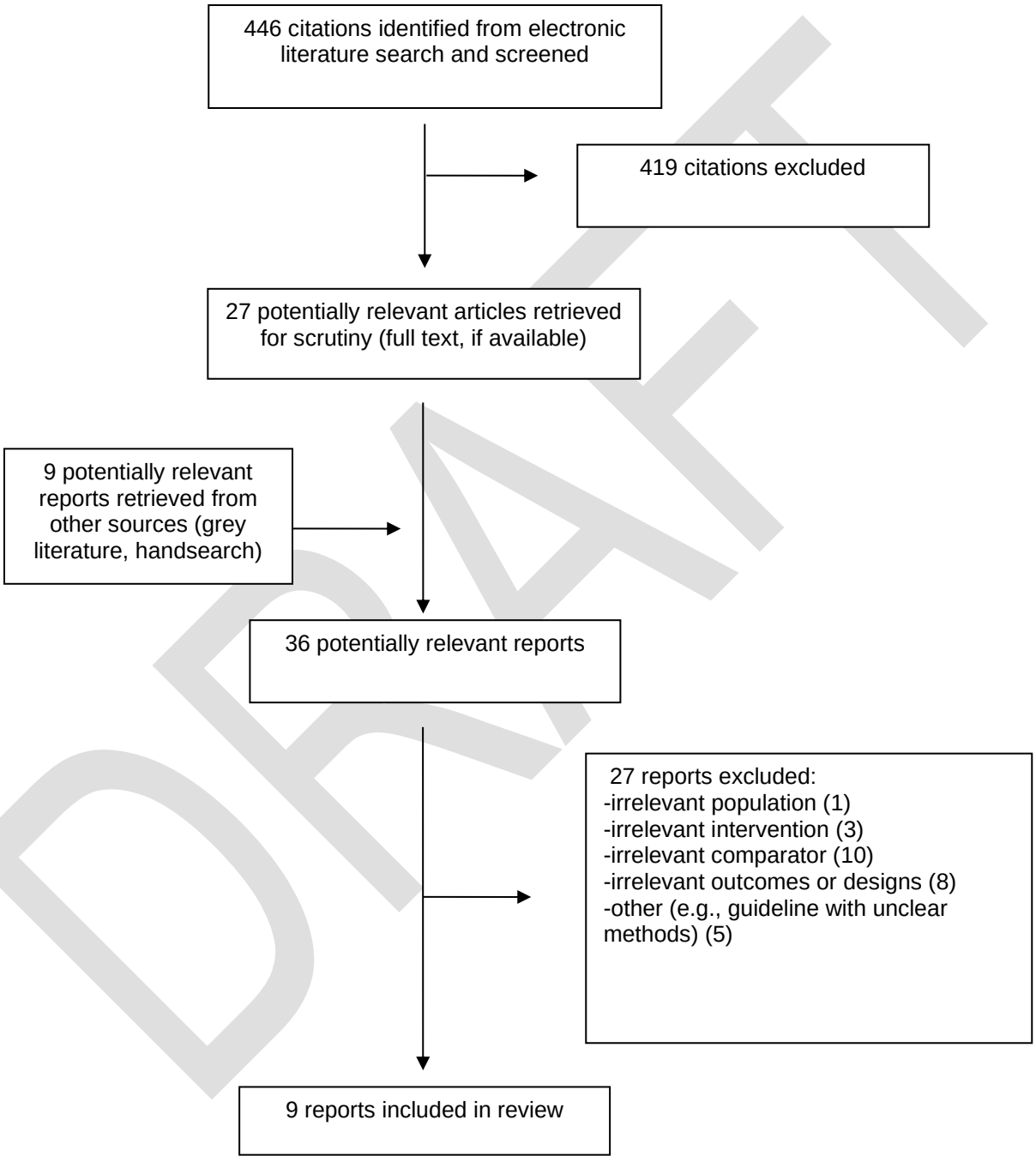
Engagement Activities

They were provided with a brief background to the project via email and in a Zoom call when requested. Two patients preferred to meet via a 1 hour Zoom call to share their experience and one patient chose to respond to the questions via email. We reported the patient involvement results using the Guidance for Reporting Involvement of Patients and the Public (version 2) Short Form reporting checklist,[43] which is outlined in Appendix 5.

This updated report is now posted for public feedback. All feedback received will be carefully considered by the research team and addressed within the report. Both clinical experts and patient partners will be invited to review the finalized version of the updated rapid review prior to publication.

Figure 1: Selection of Included Studies

Alt text: 446 citations were identified, 419 were excluded, while 27 electronic literature and 9 grey literature potentially relevant full text reports were retrieved for scrutiny. In total 9 reports are included in the review.



Appendix 2: Characteristics of Included Publications

Table 2: Characteristics of Included Systematic Reviews

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Plotas et al. (2024)[28] Greece **Funding source:** Research Council of the University of Patras	Study design: systematic review of observational studies Number of included studies: 9 Country: NR Search: up to May 2023	Patients after total laryngectomy Number of participants: from 18 to 133 Mean age: NR Age range: 45 years or over Sex: NR Disease duration: NR Radiotherapy: NR	**Intervention:** Esophageal voice without VPs **Comparator**: Voice prosthesis rehabilitation	**Outcomes:** • VHI • VRQOL • SF-36 • EORTC QLQ-C30 • EORTC QLQ-H&N35 • UW-QOL • FACT-G • GESQ • HADS • P-SECEL **Follow-up**: NR
Maniaci et al. (2024)[24] Belgium **Funding source:** NR	Study design: systematic review of observational studies Number of included studies: 15 Country: NR Search: from Dec 1, 2001 to Jun 1, 2021	Patients after total laryngectomy for advanced laryngeal cancer Number of participants: 1085 Mean age: 65.38 years Sex: male, 89.38% Disease duration: NR Radiotherapy: NR	**Intervention:** Voice prosthesis (indwelling and non-indwelling devices) rehabilitation (n=869, 80.1%) **Comparator**: esophageal voice without VPs (n=216, 19.9%)	**Outcomes:** • VHI • VRQOL • SF-36 **Follow-up**: NR
Ahmed et al. (2023)[25] Netherlands **Funding source:** Atos Medical	Study design: Mixed Methods Study with a rapid review Number of included studies: 10: 3 RCTs, 3 time-series studies, 1 retrospective	Patients who underwent total laryngectomy Number of participants: 550 (number in the	**Intervention:** HMEs (Assumption: HMEs were used in combination with VPs)	**Outcomes:** • Breathing • QOL • Mucus production or plugging • Coughing • Forced expectorations

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
	cohort study, 1 study with unclear design Country: United States, Canada, France, Italy, Spain, the Netherlands, and Poland Search: from January, 2010 to February, 2021	individual studies ranged from 30 to 89) Age: NR Sex: NR Disease duration: NR Radiotherapy: NR	**Comparator**: no HME use, an external humidifier or a previous generation HME	• Sleep quality • Psychosocial aspects • Physiotherapy • Tracheobronchitis or pneumonia episodes • Social contacts • Patient satisfaction **Follow-up**: 3 months or NR
Mayo-Yanez et al. (2023)[26] Spain **Funding source:** No funding support and the authors declared no conflict of interest	Study design: systematic review of observational studies Number of included studies: 4: 2 prospective case series, 1 prospective case-crossover, 1 case report Country: Germany, Netherlands, and Spain Search: from January, 2016 (year of the intervention commercialization) to February, 2020 (the paper was submitted in 2020 and was published in 2023)	Patients with laryngectomy and users of VP Number of participants: 55 patients (315 VP) Mean age: 62.71 Sex: male: 87.27% Disease duration: NR Radiotherapy: 55% to 100% when reported.	**Intervention:** PVX (n = 94). **Comparator**: control VP (Vega and ActiValve Light, n=221)	**Outcomes:** • VP duration **Follow-up**: NR

Study citation, country, funding source	Study designs and numbers of primary studies included	Population characteristics	Intervention and comparator(s)	Clinical outcomes, length of follow-up
Tawfik et al. (2021)[27] Egypt **Funding source:** NR	Study design: systematic review and network meta-analysis Number of included studies: 120 in network meta-analysis; 27 in meta-analysis only Country: Australia, Belgium, Brazil, Canada, China, Croatia, Czech Republic, Denmark, UK, Egypt, Finland, France, Germany, Slovakia, Greece, India, Italy, Japan, Netherlands, Norway, Pakistan, Poland, South Africa, Spain, Sweden, Switzerland, Turkey, USA. Search: up to May 11, 2019	Patients who underwent total laryngectomy Number of participants: 11,918 Mean age: 17 to 90 years Sex: male: 71.7% Disease duration: NR Radiotherapy: 71.7%.	**Intervention and comparators:** various VPs that include Provox-1, Provox-2, Provox AV, Provox NID, Provox Vega, SPVP, Nijdam, Groningen LR , Groningen ULR, BS-LP,	**Outcomes:** Devices replacements; Devices lifetime; Airflow resistance; MPT; Leakage rates; Speech rate; Patient device Preference; Phonatory effort; Voice speech quality; Fundamental frequency; Voice loudness; Speech intelligibility; Stoma Stenosis; Dislodgement; Fistula problems; Granulation; Prosthesis inaccurate size; Prosthesis deterioration; Survival rate; Aspiration pneumonia; Fungal colonization; Experience with speaking; Skin irritation; Chemoprophylaxis. **Follow-up**: from 0.5 to 133 months

AV = ActiValve; BS-LP = Blom-Singer low pressure; EORTC QLQ-C30 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-C30; EORTC QLQ-H&N35 = European Organization for Research and Treatment of Cancer Quality of Life Questionnaire-HEAD & NECK CANCER35; FACT-G = Functional Assessment of Cancer Therapy-General; GESQ = Groningen Enjoyment of Speech Questionnaire; HADS = Hospital Anxiety and Depression Scale; HMEs = Heat and moisture exchangers; LR = Low Resistance; MPT = maximum phonation time; NID = non-indwelling device; NR= Not reported; P-SECEL = Portuguese Self Evaluation of Communication Experiences after Laryngectomy Cancer Questionnaire; PVX = Provox Vega XtraSeal; QOL= Quality of life; RCT= Randomized controlled trial; SF-36 = 36-Item short form survey instrument; SPVP = Sound-Producing Voice Prosthesis; ULR = Ultra Low Resistance; UW-QOL = University of Washington Quality of Life; VHI = Voice handicap index; VP = Voice prostheses; VRQOL = Voice-related quality of life.

Table 3: Characteristics of Included Economic Evaluation

Study citation country, funding source	Type of analysis, time horizon, perspective	Population characteristics	Intervention and comparator(s)	Approach	Source of clinical, cost, and utility data used in analysis	Main assumptions
Rodriguez-Lorenzana et al. (2023)[29]	**Type of Analysis:** Cost-effective analysis	**Inclusion Criteria:** Patients who were laryngectomized,	**Intervention**: Provox XtraSeal®	**Outcome measures:** The incremental	The study included the direct medical costs, such as the cost of the	The anticipated change rate for Provox Vega® and Provox

Study citation country, funding source	Type of analysis, time horizon, perspective	Population characteristics	Intervention and comparator(s)	Approach	Source of clinical, cost, and utility data used in analysis	Main assumptions
Spain **Funding source:** covered by Fundación Profesor Nóvoa Santos (Hospital Teresa Herrera, 1ª Planta)	based on a cross-over prospective observational study **Time Horizon:** NR, but likely within study **Perspective:** Spanish national health system	18+, at least 3 months post-total laryngectomy, at least 3 months post-radiotherapy or chemotherapy, at least 3 years of follow-up, treated with proton-pump inhibitors, and had at least 3 months' experience using the Provox Vega® 38 patients, 35 men and 3 women Mean age: 66.26 ± 9.36 years old	**Comparator**: Provox Vega®	cost-effectiveness ratio (ICER) was calculated	prostheses, which were obtained from the hospital's economic department. The cost of each Provox Vega® was EUR 363 and, for Provox XtraSeal, a range between EUR 400 and EUR 600 was selected depending on the health center assessed	XtraSeal® was estimated at 3.5 changes per year. The predicted price for Provox Vega® was 1269.08 EUR and 1928.55 EUR for Provox XtraSeal®. The cost-effectiveness analysis aimed to achieve equal costs between the two devices.
Miguel Mayo-Yanez et al. (2022)[30] Spain **Funding source:** Information not available	**Type of analysis:** CEA based on prospective case-crossover study **Time Horizon:** NR, but likely within study (mean follow-up: 5.24 years, from 4.04 years to 6.57 years) **Perspective:** Spanish Public National Health System	Total laryngectomized patients with Provox Vega® and endoprosthesis leakage to whom a Provox ActiValve® was placed. 5 Caucasian men, with a mean follow-up of 5.24 years (range 4.04–6.57), were selected. Mean age: 63.84 ± 0.38 years.	**Intervention:** Provox Activalve **Comparator:** Provox Vega	**Outcome measures:** ICER was calculated A 4 quadrant cost effectiveness plane was presented	Cost of each Provox Vega: 363€, Cost of each Provox ActiValve:1,757.47€. The effectiveness of the treatment was estimated based on number of annual VP replacements and according to follow-up length.	The anticipated change rate for Provox Vega® and Provox ActiValve was estimated at 2.94 changes per year. The predicted price for Provox Vega® was 1067.60 € and 5168.82 € for Provox ActiValve.

Study citation country, funding source	Type of analysis, time horizon, perspective	Population characteristics	Intervention and comparator(s)	Approach	Source of clinical, cost, and utility data used in analysis	Main assumptions
Beck et al. (2020)[31] United States **Funding source:** information not available	**Type of analysis:** cost-effectiveness and budget impact analysis **Perspective**: The model was based on a US healthcare and societal perspective. **Time horizon:** 20 years	Participants: 40 HME-users and 22 ASC-users 47 males and 15 females **Mean age**: HME patients 65.4 (37.9-88.9); ASC patients 67.7 (40.7-88.6)	**Intervention**: heat moisture exchanger **Comparator;** alternative stoma cover	Study questionnaire was based on the Ackerstaff-Hilgers questionnaire A Markov decision model was developed with three mutually exclusive health states, reflecting the disease trajectory. **Outcome measures:** The incremental cost-effectiveness ratio was used to evaluate the cost-utility of the HME system; represents the additional costs of HME use per QALY gained.	Utilities were obtained from the EQ-5D-5L (US tariff was used) **Model inputs; clinical variables:** (device/equipment use, occurrence of pulmonary events, symptoms, productivity loss, treated with medication **costs:** annual device costs, cost of accessories and equipment were included in the model. Hospital costs and medication costs were also obtained. All costs were calculated in US dollars **health effects:** QALYs - survival probabilities after laryngectomy were derived from literature and assumed to be similar for both groups. In this analysis, disutilities were applied for progressive disease, daily extensive coughing, and mucus production per week.	The Markov model has a hypothetical cohort of 5000 patients and all simulated patients in both groups start at disease-free survival.

ASC= Alternative stoma covers; CEA = Cost-effectiveness analysis; HMEs = Heat and moisture exchangers; ICER= Incremental cost-effectiveness ratio; QALYs= quality-adjusted life years; NR = not reported; RCT= randomized controlled trials; US= United States; VP = Voice prosthesis.

Table 4: Characteristics of Included Guidelines

Intended users, target population	Intervention and practice considered	Major outcomes considered	Evidence collection, selection, and synthesis	Evidence quality assessment	Recommendations development and evaluation	Guideline validation
Mayo-Yanez et al. (2024)[32]						
Intended users: healthcare professionals: otorhinolaryngology specialists (physicians and residents), speech therapists, nursing staff, and other specialists **Target population**: Laryngectomized patients **Country:** Spain	Laryngectomized patients who are or could be users of voice prostheses	Vocal outcomes, quality of life, and complications.	The guideline authors searched MEDLINE, Embase, Scopus, Web of Science, PubMed, Science Citation Index, and The Cochrane Library between 1980 to 2023 and conducted a systematic review with 91 studies.	The Oxford Levels of Evidence system 2011: 1a: systematic review of RCTs or n-of-1 trials; to 5 (mechanism-based reasoning).	The recommendations were developed after reviewing and analyzing the most recent research: benefits, side effects, and risks. Grade of Recommendation: B or C, but the meaning of the grade of recommendation is not specified. The authors drafted and reviewed the recommendations. They used a mini-Delphi method with 2 meetings to define them.	The recommendations were then sent to the entire working group for anonymous feedback and reviewed in subsequent meetings. The guideline panel included otolaryngologists, head and neck surgeons, and expert speech therapists. The guideline was published in a peer-reviewed journal.

RCT= randomized controlled trials.

Appendix 3: Critical Appraisal of Included Publications

Table 5: Strengths and Limitations of Systematic Reviews Using AMSTAR 2[39] and the ISPOR Questionnaire[40]

Strengths	Limitations
Plotas et al. (2024)[28]	
• The purpose of the study was clearly described. • Multiple databases were searched (PubMed, Google Scholar, and Speech Bite). • The keywords in the search strategy were provided. • A flow chart of study selection was provided. • The details of the included studies were described. • The review authors assessed the studies' RoB using the Critical Appraisal Skills Programme checklists. • The study designs of the individual studies for inclusion were clearly described.	• The authors did not search the EMBASE. • A grey literature search was not reported. • The authors did not report manually searching related references from the lists of identified full texts. • The list of excluded studies was not provided. • **It was unclear if the study selection, data extraction, and RoB assessments were conducted by at least two authors independently.** • The review authors did not report details on quality-of-life measures, particularly not clarifying whether a higher score indicates better or worse quality of life for each outcome measure. • In Table 2, the authors provided p-values in the "results" column. However, it is unclear for some studies which comparisons these p-values correspond to (e.g., between-group or before-after comparisons). • The follow-up of outcome measures was unclear. • **The review authors stated that they excluded studies with risks of bias and did not conduct further analyses on the impact of risk of bias on the outcome interpretations**.
Maniaci et al. (2024)[24]	
• The purpose of the study was clearly described. • Multiple databases were searched (PubMed, Scopus, and Web of Science). • The keywords in the search strategy were provided. • The authors manually searched for related references from the lists of identified full texts. • A flow chart of study selection was provided. • The details of the included studies were adequately described. • The review authors assessed the studies' RoB using the Joanna Briggs Institute critical appraisal checklist for observational studies. • The intervention and study designs of the individual studies for inclusion were clearly described. • The authors used the GRADE framework to assess the overall certainty of evidence.	• The authors did not search EMBASE. • A grey literature search was not reported. • The list of excluded studies was not provided. • **It was unclear if the study selection, data extraction, and RoB assessments were conducted by at least two authors independently.** • The review authors did not report the funding sources and conflict of interest. • **The methods to pool all outcome measures were unclear.** • The follow-up of outcome measures was unclear. • The review authors did not assess the potential impact of RoB in individual studies on result interpretations. • **The GRADE assessment details were unclear: the starting point of the certainty of evidence from observational studies should be "low" rather than**

Strengths	Limitations
	"very low" and did not assess the certainty at the outcome level (Table 2) • There is a discrepancy between the description in the main text (p. 539.e13) on SF-36 and figure 4C.
Ahmed et al. (2023)[25]	
• The purpose of the study was clearly described. • The keywords in the search strategy were provided. • The title and abstract screening were conducted by at least two authors independently. • One reviewer performed the full-text screening and data extractions and verified them with a second reviewer. • The study designs of the individual study for inclusion were provided. • The review authors declared no conflicts of interest.	• **The authors only searched PubMed.** • A grey literature search was not reported. • The list of excluded studies was not provided. • **The authors did not assess the RoB for eligible studies.** • The details of participants, intervention and control were not clearly reported. • The follow-up of outcome measures was unclear for most outcomes. • Atos Medical provided funding support for the study.
Mayo-Yanez et al. (2023)[26]	
• The purpose of the study was clearly described. • The study designs of the individual study for inclusion were clearly described. • Multiple databases (PubMed/MEDLINE, the Cochrane Library, Google Scholar, Scielo, and Web of Science) were searched. • The keywords of the search strategy were provided. • The authors manually searched for related references from the lists of identified full texts. • The data extraction was conducted independently by two authors. • The review authors assessed the methodological quality of eligible studies, using the NICE public health guidance tool. • A flow chart of study selection was provided. • The review authors declared no conflicts of interest.	• The review authors did not search the EMBASE. • Preprint studies and gray literature were not considered. • **It was unclear if the study selection and RoB were conducted by at least two authors independently.** • The list of excluded studies was not provided. • **The details of participants, intervention and control were not clearly reported.** • The follow-up of outcome measures was unclear for most outcomes.
Tawfik et al. (2021)[27]	
• The purpose of the study was clearly described. • The protocol of this review was prospectively registered in the PROSPERO (CRD42017080110). • Multiple databases were searched (PubMed, Google Scholar,Scopus, Web of Science, EMBASE, VHL, WHO GHL, Cochrane, Clinical trials.gov, mRCT, Science Direct, WHO, CINAHL, POPLINE, and SIGLE). • The search strategies were provided in supplemental Table S2. • A manual search of possibly missing articles was conducted. • The study selection process and data extraction were clearly described and conducted by 3 reviewers. • The review authors assessed the RoB for RCTs using the Cochrane Collaboration RoB tool; for	• There are several discrepancies between the registered systematic review protocol in PROSPERO (CRD42017080110) and the published reviews. • The review authors did not report the funding sources for eligible studies. • The review authors did not assess the potential impact of RoB in individual studies on result interpretations. • **The ranks of the best interventions for each outcome were based on p-scores only, without considering the certainty of evidence.** • The review authors did not report the funding sources and conflict of interest. • **This network included observational studies.** • The review did not report direct and indirect estimates.

Strengths	Limitations
observational studies using the National Institutes of Health for observational cohort, cross-sectional studies, and case-series studies. • A flow chart of study selection was provided. • Publication bias assessments were conducted. • The characteristics of the included studies were adequately described. • The network plot was presented in the appendix. • The pointed estimates and 95% credible intervals were reported.	• **The authors did not assess the systematic differences in treatment effect modifiers across the different treatment comparisons in the network.** • The individual study results and the details of outcome measures were not reported. • The impact of important patient characteristics (e.g., age or disease severity) on treatment effects were not reported. • **The conclusions did not consider the results of statistical tests and the certainty of evidence.**

AMSTAR 2 = A MeaSurement Tool to Assess systematic Reviews 2; CCAT= Crowe Critical Appraisal Tool; CINAHL = Cumulative Index to Nursing and Allied Health Literature; GRADE= Grading of Recommendations, Assessment, Development and Evaluation; ISPOR = Questionnaire to assess the relevance and credibility of a network meta-analysis; mRCT = metaRegister of Controlled Trials; POPLINE = Population Information Online; RCTs= Randomized controlled trials; RoB= risk of bias; SIGLE = System for Information on Grey Literature in Europe; VHL = Virtual Health Library; WHO = World Health Organization; WHO GHL= World Health Organization Global Health Library.

Table 6: Strengths and Limitations of Economic Evaluation Using the Drummond Checklist [41]

Strengths	Limitations
Rodriguez-Lorenzana et al. (2023)[29]	
Study design • The research question, type of economic evaluation, viewpoint of the analysis are clearly stated • Description of the alternatives and rationale for alternatives are clear **Data Collection** • Source of effectiveness estimates are stated • Primary outcome measures for the economic evaluation clearly stated • The design and results of the effectiveness study were given • Characteristics of study participants included in the analysis were described • Currency and cost reported • Quantities of resource use are reported separately from unit costs, and methods of estimating costs are mentioned **Analysis and interpretation:** • Incremental analyses provided • Intervention and comparator were compared • Answer to study question is given • Conclusions follow from the data reported and accompanied by appropriate caveats • Major outcomes reported in disaggregate and aggregate form	• The economic importance of the research question were not described • Use of cost effectiveness models were not described • Time horizon in the cost effectiveness model was not stated. • Details of currency of price adjustments for inflation or currency conversion were not given. • No information on discount rate provided • Information on stochastic data not provided • No sensitivity analysis was conducted.
Mayo-Yáñez et al. (2022)[30]	

Strengths	Limitations
Study design • Research question, economic importance of research question, viewpoint of analysis clearly stated • Intervention and comparator clearly described • Type of economic evaluation was stated **Data Collection** • Source of effectiveness and details of the design and results of effectiveness study are given • primary outcome measure(s) stated for economic evaluation • details of subjects included in analysis were given • Quantities of resource use listed separate from cost • Currency and price data recorded **Analysis and interpretation:** • Relevant alternatives are compared • incremental analysis reported • Answer to research question and conclusions from data reported, accompanied by appropriate caveats • Major outcomes reported in disaggregate and aggregate form	• Method of estimation of quantities/unit costs not fully described • Use of cost effectiveness models were not described • Time horizon in the cost effectiveness model was not clearly stated. • Details of currency of price adjustments for inflation or currency conversion are not given. • Explanation not given for why costs and benefits not discounted • Sensitivity analysis not performed • No information on discount rate provided • Information on stochastic data not provided
Beck et al. (2020)[31]	
Study design • Research question and economic importance of the question is stated • Viewpoints of analysis clearly stated • Alternatives being compared are clearly described • Form of economic evaluation is stated **Data Collection** • Source of effectiveness estimates are stated • Detail of design and results of effectiveness study are given • Primary outcome measures for evaluation clearly stated • Methods to value benefits are stated • Details of participants in analysis were given • Productivity changes reported separately • Currency and price data are recorded • Details of model used given and choice of model and key parameters are justified **Analysis and interpretation:** • Time horizon of costs and benefits stated • Discount rate (3%) is provided • Details of statistical tests and confidence intervals are given for stochastic data. • Approach to sensitivity analysis is provided and choice of variables are justified • Relevant alternatives compared • incremental analysis reported • Major outcomes reported in disaggregate and aggregate form	• Details of currency of price adjustments for inflation or currency conversion are not given. • Choice of discount rate not explicitly justified but a citation is provided

Strengths	Limitations
• Conclusions follow from data reported and accompanied by appropriate caveats	

Table 7: Strengths and Limitations of Guidelines Using AGREE II[42]

Item	Mayo-Yanez et al (2024)[32]
Domain 1: scope and purpose	
1. The overall objective(s) of the guideline is (are) specifically described.	Yes
2. The health question(s) covered by the guideline is (are) specifically described.	Yes
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	Yes
Domain 2: stakeholder involvement	
4. The guideline development group includes individuals from all relevant professional groups.	Yes
5. The views and preferences of the target population (patients, public, etc.) have been sought.	No
6. The target users of the guideline are clearly defined.	Yes
Domain 3: rigour of development	
7. Systematic methods were used to search for evidence.	Yes
8. The criteria for selecting the evidence are clearly described.	Yes
9. The strengths and limitations of the body of evidence are clearly described.	Yes
10. The methods for formulating the recommendations are clearly described.	Yes
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.	To some extent but lacked details.
12. There is an explicit link between the recommendations and the supporting evidence.	No
13. The guideline has been externally reviewed by experts prior to its publication.	NR

Item	Mayo-Yanez et al (2024)[32]
14. A procedure for updating the guideline is provided.	No
Domain 4: clarity of presentation	
15. The recommendations are specific and unambiguous.	No
16. The different options for management of the condition or health issue are clearly presented.	No
17. Key recommendations are easily identifiable.	Yes
Domain 5: applicability	
18. The guideline describes facilitators and barriers to its application.	Partially mentioned facilitators
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.	No
20. The potential resource implications of applying the recommendations have been considered.	No
21. The guideline presents monitoring and/or auditing criteria.	No
Domain 6: editorial independence	
22. The views of the funding body have not influenced the content of the guideline.	Unclear (Atos Medical funded this guideline, and one of the co-authors is an employee of Atos Medical.)
23. Competing interests of guideline development group members have been recorded and addressed.	Yes (the authors declare no conflicts of interest)

AGREE II = Appraisal of Guidelines for Research and Evaluation II; NR = not reported.

Appendix 3: Main Study Findings

Table 8: Summary of Findings by Outcome—Quality of Life for TEV versus EV

Author (Year) and Study Design	Results				
	Group (number of studies or participants) or variables	Effect measure	Effect estimate	I^2 (%)	Notes
VHI (The range and direction of total scores were not reported)					
Maniaci et al. (2024)[24] Systematic review with 15 studies	TEV (9 studies)	Pooled Mean (SD), points	31.93 (12.11)	NA	P = 0.003
	EV (9 studies)	Pooled Mean (SD), points	35.39 (20.6)	NA	
	Comparison between TEV and EV (5 studies)	MD (95% CI), points	-1.90 (-14.83 to 11.02)	97%	Random-effects model
VRQOL (The range and direction of total scores were not reported)					
Maniaci et al. (2024)[24] Systematic review with 15 studies	TEV (7 studies)	Pooled Mean (SD), points	8.27 (5.98)	NA	NS
	EV (7 studies)	Pooled Mean (SD), points	9.27 (2.02)	NA	
	Comparison between TEV and EV (3 studies)	MD (95% CI), points	-0.74 (-2.85 to 1.38)	71%	Random-effects model
SF-36 (The range and direction of total scores were not reported)					
Maniaci et al. (2024)[24] Systematic review with 15 studies	TEV (4 studies)	Pooled Mean (SD), points	58.7(2.94)	NA	P < 0.001
	EV (4 studies)	Pooled Mean (SD), points	61.84 (8.33)	NA	

CI = confidence interval; EV = esophageal voice; NA= not applicable; NS = not statistically significant; SD= Standard deviation; SF-36 = 36-Item short form survey instrument; TEV = tracheoesophageal voice; VHI = Voice handicap index; VP = Voice prostheses; VRQOL = Voice-related quality of life.

Table 9: Summary of Findings- Various clinical outcomes for HMEs versus non-HMEs

Author (Year) and Study Design	Results				
	Number of studies	Outcome/Effect measure	Effect estimate	P	Notes
QOL (The range and direction of total scores were not reported)					
Ahmed et al. (2023)[25] Study design: mixed methods study with a rapid review with 10 studies	QOL (Shortness of breath)				
	1 study (Brook et al 2013)	QOL questionnaire (unclear tool), points	Non-HME: 4.6 Provox Micron HMEs (first generation): 4.9 Provox HME (first generation): 4.3	0.363	NS
	QOL (Sleep quality)				
	1 study (Brook et al 2013)	QOL questionnaire (unclear tool), points	Non-HME: 4.5 Provox Micron HMEs (first generation): 4.8 Provox HME (first generation): 4.6	0.913	NS
	QOL (Speech quality)				
	1 study (Brook et al 2013)	QOL questionnaire (unclear tool), points	Non-HME: 7.6 Provox Micron HMEs (first generation): 9.4 Provox HME (first generation): 8.0	0.396	NS
	QOL (Psychosocial aspects)				
	1 study (Brook et al 2013)	QOL questionnaire (unclear tool), points	Non-HME: 5.8 Provox Micron HMEs (first generation): 6.5 Provox HME (first generation): 6.6	0.688	NS
	QOL (social contacts)				
	1 study (Brook et al 2013)	QOL questionnaire (unclear tool), points	Non-HME: 9.6 Provox Micron HMEs (first generation): 8.4 Provox HME (first generation): 9.7	0.438	NS
Mucus production					
Ahmed et al. (2023)[25] Study design: mixed methods study with a rapid review with 10 studies	1 study (Ebersole et al 2020)	rate of mucus production	XtraHME: 0.13 per 10 inpatient days EH：0.38 per 10 inpatient days	P=0.02	Statistically lower in the XtraHME group
	1 study (Ebersole et al 2020)	proportion of patients with ≥1 mucus plug events	XtraHME: 11% EH： 50%	P=0.01	statistically reduced in the XtraHME group
	1 study (Foreman et al 2016)	proportion of patients experiencing mucus plugging	HME: 12.5% EH： 87.5%	P=0.002	Odds ratio of a mucus plug event when not using HME:

Author (Year) and Study Design	Results				
	Number of studies	Outcome/Effect measure	Effect estimate	P	Notes
					8.27 (confidence interval not reported).
Coughing					
Ahmed et al. (2023)[25] Study design: mixed methods study with a rapid review with 10 studies	1 study (Dassonville et al 2016)	Coughing (an analog scale ranging from 0 to 10), points	"At 3 months, there was a significant decrease in coughing in the HME group versus the no-HME control group." (p. 5)	P=0.00174	statistically decreased in the HME group
	1 study (Bień et al 2010)	frequency of coughing	HME: week 1: 48 times; week 12: 30 times Control: week 1: 60 times; week 12: 56 times	<0.001	statistically decrease in the HME group
	1 study (Mérol et al)	number of coughing episodes	"In the EH group, 73% of the patients had 2 to 10 spontaneous coughing episodes per day, whereas 8% had 20, another 8% had 30, and 4% had 72 episodes a day (for 8%, this information was missing). In the HME group, most patients (90%) had 1 to 5 spontaneous coughing episodes per day, whereas 4.3% had 10 and another 4.3% had 20 such episodes per day" (p.6)	<0.001	significantly lower in the HME group
Forced expectorations					
Ahmed et al. (2023)[25] Study design: mixed methods study with a rapid review with 10 studies	1 study (Bień et al 2010)	frequency of forced expectorations	HME: week 1: 56 times; week 12: 27 times Control: week 1: 59 times; week 12: 53 times	<0.001	statistically decreased in the HME group
Sleep Quality					
Ahmed et al. (2023)[25]	1 study (Foreman et al 2016)	Sleep quality (unclear tool)	"No significant difference was reported between the HME group and EH group in sleep quality" (p.6)	NR	NS

Author (Year) and Study Design	Results				
	Number of studies	Outcome/Effect measure	Effect estimate	P	Notes
Study design: mixed methods study with a rapid review with 10 studies	1 study (Bień et al 2010)	frequency of patients who had sleeping problems	"In the control group, almost all the patients (97.5%) had sleeping problems, and this did not change over time. In the full compliance HME group (first generation), 79% of the patients had sleeping problems at baseline, and 72% had this problem after 3 months of HME use." (p. 6)	NR	NS
Speech Quality					
Ahmed et al. (2023)[25] Study design: mixed methods study with a rapid review with 10 studies	1 study (Brook et al 2013)	Speech quality (unclear tool)	"The HME users and Micron users reported a better voice than did the non-HME users (not statistically significant)" (p.6)	NR	NS
Physiotherapy					
Ahmed et al. (2023)[25] Study design: mixed methods study with a rapid review with 10 studies	1 study (Foreman et al 2016)	the number of days requiring chest physiotherapy after surgery	Provox XtraHME: 1.75 days EH: 3.20 days	0.034	significantly reduced in the HME group
Tracheobronchitis or pneumonia episodes					
Ahmed et al. (2023)[25] Study design: mixed methods study with a rapid review with 10 studies	1 study (van den Boer et al 2014)	tracheobronchitis or pneumonia episodes	HME (first generation): 0.066 episodes per patient per year Non-HME: 0.285 episodes per patient per year	0.047	statistically lower in the HME group
	1 study (van den Boer et al 2014)	Pulmonary infections (tracheobronchitis and pneumonia together)	HME (first generation): 0.092 episodes per patient per year Non-HME: 0.129 episodes per patient per year	0.33	NS
Social contacts					

Author (Year) and Study Design	Results				
	Number of studies	Outcome/Effect measure	Effect estimate	P	Notes
Ahmed et al. (2023)[25] Study design: mixed methods study with a rapid review with 10 studies	1 study (Parrilla et al 2015)	Unclear tool (after 12 weeks), points	"A statistically nonsignificant improvement in social contacts, with a baseline value of 8.1 versus a value 8.3 after 12 weeks (P=.728), was reported in the structured questionnaires when comparing no HME use with HME (second generation) use." (p. 7)	0.728	NS
Patient Satisfaction					
Ahmed et al. (2023)[25] Study design: mixed methods study with a rapid review with 10 studies	1 study (Mérol et al 2012)	Unclear tool	"Patients' satisfaction showed a significant improvement of first-generation HME over EH (P<.001). Patient satisfaction with the EH was quite low: 11% of the patients reported that they were satisfied with it, 8% reported they somewhat liked it, and 81% reported that they did not like it. All the patients (100%) in the HME (first generation) group were satisfied with the device" (p. 7)	<0.001	statistically improvement in the HME group over EH.

EH = external humidifier; HME = heat and moisture exchanger; NR= not reported; NS= not statistically significant; QOL = quality of life.

Table 10: Summary of Findings by Outcome — Device replace frequency

Author (year) and study design	Results			
	VP device	Comparator VP	Effect estimate: RR (95% CI)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (27 studies with 5724 patients)	Provox-1	BS-LP	0.69 (0.19 to 2.51)	NS
	Nijdam	BS-LP	0.78 (0.09 to 6.73)	NS
	Groningen ULR	BS-LP	0.81 (0.07 to 9.14)	NS
	Provox AV	BS-LP	0.96 (0.09 to 10.74)	NS
	Provox NID	BS-LP	1.24 (0.17 to 9.07)	NS
	Provox Vega	BS-LP	1.24 (0.17 to 9.11)	NS
	Provox 2	BS-LP	1.30 (0.30 to 5.58)	NS

Author (year) and study design	Results			
	VP device	Comparator VP	Effect estimate: RR (95% CI)	Notes
	Groningen LR	BS-LP	1.44 (0.30 to 7.03)	NS
	SPVP	BS-LP	10.10 (0.71 to 144.07)	NS

AV = ActiValve; BS-LP = Blom-Singer low pressure; CI = confidence interval; LR = Low Resistance; NID = non-indwelling device; NS = not statistically significant; RR= relative risk; SPVP = Sound-Producing Voice Prosthesis; VP = voice prosthesis.

Table 11: Summary of Findings by Outcome — Device lifetime

Author (year) and study design			Results	
	Comparisons	Effect measure	Effect estimate (years)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (33 studies with 4777 patients)	Provox-AV vs. BS Advantage	MD (95% CI)	17.25 (0.40 to 34.09)	Statistically significant (p value was not reported)
	Nijdam vs. BS Advantage	MD (95% CI)	9.87 (-6.67 to 26.42)	NS
	Provox 1 vs. BS Advantage	MD (95% CI)	9.00 (-7.24 to 25.25)	NS
	Groningen LR vs. BS Advantage	MD (95% CI)	8.44 (-7.76 to 24.65)	NS
	Groningen ULR vs. BS Advantage	MD (95% CI)	7.45 (-9.18 to 24.09)	NS
	BS DV vs. BS Advantage	MD (95% CI)	6.30 (-19.12 to 31.72)	NS
	Provox 2 vs. BS Advantage	MD (95% CI)	6.82 (-9.26 to 22.91)	NS
	Provox Vega vs. BS Advantage	MD (95% CI)	5.24 (-10.87 to 21.36)	NS
	BS-LP vs. BS Advantage	MD (95% CI)	4.97 (-11.09 to 21.03)	NS
Mayo-Yáñez et al. (2023)[26] Systematic review with 4 studies	PVX vs. Control VP (Vega or ActiValve light)	Mean ± SD (95% CI)	PVX: 114.28 ± 73.2 (98.29 to 130.26) days Control: 102.98 ± 17.74 (100.6 to 105.35) days	No statistical test performed

AV = ActiValve; BS-LP = Blom-Singer; CI= confidence interval; DV = Dual valve; LP = loe pressure; LR = Low Resistance; MD = mean difference; NR= Not reported; NS= not statistically significant; PVX = Provox Vega XtraSeal; ULR = Ultra Low Resistance.

Table 12: Summary of Findings by Outcome — Air flow resistance

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: RR (95% CI)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (8 studies with 1850 patients)	Provox 2	Groningen LR	0.42 (0.08 to 2.11)	NS
	Provox 1	Groningen LR	0.84 (0.18 to 3.95)	NS
	Nijdam	Groningen LR	1.31 (0.22 to 7.67)	NS

CI= confidence interval; LR = Low Resistance; NS= not statistically significant; RR= relative risk.

Table 13: Summary of Findings by Outcome — Maximum phonation time

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: MD (95% CI), Seconds	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (13 studies with 639 patients)	Provox HME	BS Advantage	6.30 (3.34 to 9.26)	Statistically significant (p value was not reported)
	BS ATV	BS Advantage	3.00 (-0.35 to 6.35)	NS
	Provox FreeHands HME	BS Advantage	-2.90 (-6.07 to 0.27)	NS
	Provox 2	BS Advantage	-3.60 (-7.55 to 0.35)	NS
	Provox 1	BS Advantage	-5.63 (-8.99 to -2.27)	Statistically significant (p value was not reported)
	BS-LP	BS Advantage	-5.90 (-9.26 to -2.53)	Statistically significant (p value was not reported)
	Panje	BS Advantage	-7.90 (-12.14 to -3.65)	Statistically significant (p value was not reported)
	Groningen LR	BS Advantage	-12.38 (-22.69 to -2.07)	Statistically significant (p value was not reported)

ATV = Adjustable Tracheostoma Valve; BS = Blom-Singer; CI= confidence interval; HME = heat and moisture exchanger; LR= low resistance; MD= mean difference; NS= not statistically significant; VP= voice prostheses

Table 14: Summary of Findings by Outcome — Leakage

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: RR (95% CI)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (40 studies with 1493 patients)	Provox Vega	BS-LP	1.87 (0.97 to 3.60)	NS
	Provox 2	BS-LP	2.08 (1.11 to 3.88)	Statistically significant (p value was not reported)
	Nijdam	BS-LP	2.23 (1.27 to 3.90)	Statistically significant (p value was not reported)
	Groningen LR	BS-LP	2.39 (1.37 to 4.15)	Statistically significant (p value was not reported)
	Provox 1	BS-LP	3.25 (1.89 to 5.60)	Statistically significant (p value was not reported)

BS-LP = Blom-Singer low pressure; CI = confidence interval; LR= low resistance; NS= not statistically significant; RR= relative risk; VP = voice prostheses.

Table 15: Summary of Findings by Outcome — Speech rate

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: MD (95% CI) (units not reported)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (40 studies with 1493 patients)	Groningen LR	BS-LP	-1.75 (-24.67 to 21.17)	NS

BS-LP = Blom-Singer low pressure; CI = confidence interval; LR= low resistance; MD = mean difference; NS= not statistically significant; VP = voice prostheses.

Table 16: Summary of Findings by Outcome — Patient device preference

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: OR (95% CI)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (21 studies with 932 patients)	Provox 2	BS-LP	33.88 (0.65 to 1762.24)	NS
	Provox 1	BS-LP	12.04 (0.27 to 538.08)	NS
	Provox XtraHME	BS-LP	13.09 (0.18 to 974.17)	NS
	Provox HME	BS-LP	10.27 (0.54 to 194.25)	NS
	Provox Stomafilter HME	BS-LP	2.91 (0.03 to 266.18)	NS
	Groningen LR	BS-LP	1.46 (0.03 to 65.10)	NS
	Provox FreeHands	BS-LP	0.67 (0.01 to 61.92)	NS
	Provox FreeHands HME	BS-LP	0.19 (0.00 to 12.38)	NS
	VoiceMaster	BS-LP	0.10 (0.00 to 23.37)	NS
	External Humidifier	BS-LP	0.04 (0.00 to 1.22)	NS

BS-LP = Blom-Singer low pressure; CI= confidence interval; HME = heat and moisture exchanger; LR= low resistance; NS= not statistically significant; OR = odds ratio; VP= voice prostheses.

Table 17: Summary of Findings by Outcome — Increase phonatory effort

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: OR (95% CI)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (4 studies with 75 patients)	Provox Vega	BS-LP	4.11 (1.29 to 13.06)	Statistically significant (p value was not reported)

BS-LP = Blom-Singer low pressure; CI= confidence interval; NS= not statistically significant; OR = odds ratio; VP= voice prostheses.

Table 18: Summary of Findings by Outcome — Voice speech quality

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: OR (95% CI)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (6 studies with 620 patients)	Provox Vega	BS-LP	16.41 (4.33 to 62.22)	Statistically significant (p value was not reported)
	Panje	BS-LP	1.00 (0.16 to 6.08)	NS

BS-LP = Blom-Singer low pressure; CI= confidence interval; NS= not statistically significant; OR = odds ratio; VP= voice prostheses.

Table 19: Summary of Findings by Outcome — Fundamental Frequency

Author (year) and study design			Results	
	VP device	Comparator VP	Effect size: MD (95% CI) (units not reported)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (8 studies with 148 patients)	SPVP	Groningen LR	96.33 (17.29 to 175.37)	Statistically significant (p value was not reported)
	Provox 1	Groningen LR	0.08 (-4.21 to 4.36)	NS

BS-LP = Blom-Singer low pressure; CI= confidence interval; LR = low resistance; MD= mean difference; NS= not statistically significant; SPVP = Sound-Producing Voice Prosthesis; VP= voice prosthesis.

Table 20: Summary of Findings by Outcome — Voice Loudness

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: MD (95% CI) (units not reported)	Notes
	Staffieri	BS-LP	0.03 (-11.75 to 11.81)	NS

Tawfik et al. (2021)[27] Systematic review with network meta-analysis (7 studies with 247 patients)	Provox 1	BS-LP	-0.50 (-5.48 to 4.48)	NS
	Provox NID	BS-LP	-1.00 (-4.62 to 2.62)	NS

BS-LP = Blom-Singer low pressure; CI= confidence interval; LR = low resistance; MD= mean difference; NID = non-indwelling device; NS= not statistically significant; VP= voice prosthesis.

Table 21: Summary of Findings by Outcome — Speech Intelligibility

			Results	
Author (year) and study design	**VP device**	**Comparator VP**	**Effect estimate: OR (95% CI)**	**Notes**
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (7 studies with 692 patients)	Nijdam	Groningen LR	3.02 (0.12 to 74.99)	NS
	Provox 1	Groningen LR	0.10 (0.02 to 0.55)	Statistically significant (p value was not reported)

CI= confidence interval; LR = low resistance; NS= not statistically significant; OR = odds ratio; VP= voice prosthesis.

Table 22: Summary of Findings by Outcome — Stoma stenosis

			Results	
Author (year) and study design	**VP device**	**Comparator VP**	**Effect estimate: RR (95% CI)**	**Notes**
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (8 studies with 437 patients)	Provox Vega	BS-LP	5.25 (2.06 to 13.40)	Statistically significant (p value was not reported)

BS-LP = Blom-Singer low pressure; CI= confidence interval; RR= relative risk; VP= voice prosthesis.

Table 23: Summary of Findings by Outcome — Dislodgement

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: RR (95% CI)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (31 studies with 2977 patients)	Provox 2	Provox 1	0.27 (0.13 to 0.57)	Statistically significant (p value was not reported)
	Provox Vega	Provox 1	0.28 (0.12 to 0.67)	Statistically significant (p value was not reported)

CI= confidence interval; RR = relative risk; VP= voice prosthesis.

Table 24: Summary of Findings by Outcome — Fistula problems

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: RR (95% CI)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (13 studies with 1767 patients)	Groningen LR	ESKA-Herrmann	0.76 (0.50 to 1.18)	NS
	Provox 1	ESKA-Herrmann	0.87 (0.66 to 1.15)	NS
	Nijdam	ESKA-Herrmann	0.96 (0.61 to 1.51)	NS

CI= confidence interval; LR = low resistance; NS= not statistically significant; RR = relative risk; VP= voice prosthesis.

Table 25: Summary of Findings by Outcome — Granulation

Author (year) and study design			Results	
	VP device	Comparator VP	Effect estimate: RR (95% CI)	Notes
Tawfik et al. (2021)[27]	Provox 2	BS-LP	0.73 (0.02 to 26.32)	NS
	Provox 1	BS-LP	0.95 (0.13 to 7.03)	NS

Systematic review with network meta-analysis (23 studies with 3474 patients)	Provox Vega	BS-LP	0.87 (0.01 to 63.18)	NS
	VoiceMast	BS-LP	0.96 (0.06 to 15.20)	NS
	Groningen LR	BS-LP	0.97 (0.05 to 18.26)	NS
	Nijdam	BS-LP	1.93 (0.10 to 36.18)	NS

BS-LP = Blom-Singer low pressure; CI= confidence interval; LR = low resistance; NS= not statistically significant; RR = relative risk; VP= voice prosthesis.

Table 26: Summary of Findings by Outcome — Prosthesis inaccurate size

			Results	
Author (year) and study design	**VP device**	**Comparator VP**	**Effect estimate: RR (95% CI)**	**Notes**
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (4 studies with 388 patients)	Provox 2	Provox 1	0.77 (0.23 to 2.61)	NS

CI= confidence interval; NS= not statistically significant; RR = relative risk; VP= voice prosthesis.

Table 27: Summary of Findings by Outcome — Prosthesis deterioration

			Results	
Author (year) and study design	**VP device**	**Comparator VP**	**Effect estimate: RR (95% CI)**	**Notes**
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (3 studies with 200 patients)	Provox 2	Provox 1	2.62 (0.88 to 7.81)	NS

CI= confidence interval; NS= not statistically significant; RR = relative risk; VP= voice prosthesis.

Table 28: Summary of Findings by Outcome — Survival rate

Author (year) and study design	VP device	Comparator VP	Results: Effect estimate: RR (95% CI)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (3 studies with 135 patients)	Provox 1	BS-LP	1.99 (0.49 to 8.15)	NS

BS-LP = Blom-Singer low pressure; CI= confidence interval; NS= not statistically significant; RR = relative risk; VP= voice prosthesis.

Table 29: Summary of Findings by Outcome — other outcomes

Author (Year) and Study Design	Results: Group (number of studies)	Effect measure	Effect estimate (percentage)	I^2 (%)	Notes
Aspiration pneumonia					
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (4 studies with 274 patients)	Provox 2 (1 study)	Event rate (95% CI)	0.063 (0.016 to 0.218)	NA	_
	Provox 1 (1 study)	Event rate (95% CI)	0.034 (0.011 to 0.102)	NA	_
	BS-LP (2 studies)	Event rate (95% CI)	0.041 (0.019 to 0.089)	NR	_
Fungal colonization					
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (6 studies with 213 patients)	Provox 2 (1 study)	Event rate (95% CI)	0.810 (0.663 to 0.902)	NA	_
	Provox 1 (2 studies)	Event rate (95% CI)	0.652 (0.552 to 0.741)	NR	_
	BS-LP (2 studies)	Event rate (95% CI)	0.500 (0.350 to 0.650)	NR	_
Rate of patients who were fluent in speaking					
	Provox Hands-free HME ENB (1 study)	Event rate (95% CI)	0.792 (0.587 to 0.911)	NA	_

Author (Year) and Study Design	Results				
	Group (number of studies)	Effect measure	Effect estimate (percentage)	I^2 (%)	Notes
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (4 studies with 274 patients)	Provox HME (1 study)	Event rate (95% CI)	0.500 (0.342 to 0.658)	NA	_
	BS-LP (2 studies)	Event rate (95% CI)	0.480 (0.370 to 0.592)	NR	_
	Groningen LR (1 Study)	Event rate (95% CI)	0.352 (0.237 to 0.587)	NA	_
	Provox 1 (1 study)	Event rate (95% CI)	0.222 (0.056 to 0.579)	NA	_
	Provox Hands-free HME (1 study)	Event rate (95% CI)	0.208 (0.089 to 0.413)	NA	_
Skin irritation rate					
Tawfik et al. (2021)[27] Systematic review with network meta-analysis (6 studies with 213 patients)	Overall	Event rate (95% CI)	0.189 (0.113 to 0.300)	NA	_
	Provox StabiliBase (1 study) with the highest rate	Event rate (95% CI)	0.571 (0.316 to 0.794)	NA	_
	BS-LP (1 studies) with the lowest rate	Event rate (95% CI)	0.019 (0.005 to 0.074)	NA	_

BS-LP = Blom-Singer low pressure; CI= confidence interval; ENB = external neck brace; HME = heat and moisture exchanger; LR= low resistance; NA = not applicable; NR = not reported NS= not statistically significant.

Table 30: Summary of Findings of Included Economic Evaluations

Main study findings	Authors' conclusion
Rodriguez-Lorenzana et al. (2023)[29]	

• Annual replacement rates:
  • Provox Vega: 3.05
  • Provox XtraSeal: 2.05
• Effectiveness: 1.04
• Mean cost effectiveness
  • Provox Vega: EUR 2481.92
  • Provox Xtraseal: EUR 743.52
• Cost difference: EUR -938.86
• ICER (EUR/Effectiveness): -0.01
  • Lower cost scenario: -291.80
  • Higher cost scenario: 93.07
	" By reducing the number of changes needed, the Provox XtraSeal® prosthesis offers a cost-effective alternative. The positive cost-effectiveness relationship of the Provox XtraSeal® prosthesis implies that the benefits gained from using this prosthesis outweigh the associated costs" (p. 10)

Mayo-Yáñez et al. (2022)[30]	

Main study findings	Authors' conclusion

• Annual replacement rates:
  • Provox Vega: 8.16
  • Provox ActiValve: 1.15
• Effectiveness: 7.01
• Cost difference: -938.86€
• Mean cost-effectiveness
  • Provox Vega: -567.60€
  • Provox ActiValve: 1130.04€
• ICER (€/Effectiveness): -133.97
	"The results proved the significant differences in terms of prothesis duration between Provox Vega and Provox ActiValve, as week as its use is more effective and less expensive. These findings support the use of Provox ActiValve in patients with increased prosthesis replacements due to endoprosthesis leakage, to reduce the number of changes and cost." (p. 4171-4172)

Beck et al. (2020)[31]	

Healthcare perspective;
• HME:
  • Total costs per patient (USD $): 29 889
  • Total QALYs per patient: 5.30
• ASC:
  • Total costs per patient ($): 31 551
  • Total QALYs per patient: 5.15
• Incremental:
  • Total costs per patient ($): -1662
  • Total QALYs per patient: 0.14
  • ICER ($/QALY) : -11 833
  • Annual budget savings ($): 1 551 083
  • Total costs per pulmonary event averted ($): 3770
Social Perspective:
• HME:
  • Total costs per patient: 59 362
  • Total QALYs per patient: 5.3
• ASC:
  • Total costs per patient: 102 416
  • Total QALYs per patient: 5.15
• Incremental:
  • Total costs per patient: -43 054
  • Total QALYs per patient: 0.14
  • ICER ($/QALY): -306 551
  • Annual budget savings: 40 183 593
  • Total costs per pulmonary event averted: 3770
	"HME use scores favorably on cost-effectiveness compared with the ASC use in the pulmonary rehabilitation after laryngectomy in the US healthcare and societal setting." (p. 3732)

ASC= Alternative stoma covers; ICER= Incremental cost-effectiveness ratio; QALYs= quality-adjusted life years; US= United States; VP = Voice prosthesis.

Table 31: Summary of Recommendations in Included Guidelines

Recommendations and supporting evidence	Quality of evidence and strength of recommendations

Mayo-Yanez (2024)[32]	
"For the management of periprosthetic leakage, the replacement of the prosthesis with a double-flanged one, such as the Provox® Vega™ XtraSeal™, is recommended." (p. 8) (Recommendation 15) Relevant supporting evidence: "Replacement with a double-flanged prosthesis (Provox® Vega™ XtraSeal™) has shown a reduction in periprosthetic leakage (9.62% with XtraSeal vs. 22.43% in the control group) and has been shown to be a cost-effective procedure in the long term (3a, B). The Blom-Singer large oesophageal and tracheal flange VP is also a useful solution for the management of periprosthetic leakage, ensuring similar voice quality and an identical lifespan to that of other voice prostheses." (p. 9)	Recommendation: B; based on 3b evidence.
"For the management of periprosthetic leakage, VP replacement with the adjustment of diameter and length, or the placement of a silicone sheet on the tracheal side of the prosthesis, is also recommended." (p. 8) (Recommendation 16) Relevant supporting evidence: "The management of this complication is usually conservative (4, C). Initially, techniques such as adjusting the size of the prosthesis or placing a silicone ring around the tracheal face of the prosthesis are used. "(p. 8)	Recommendation: C; based on C evidence.

VP = voice prosthesis

Appendix 5: Patient Involvement

Table 32: Summary of Patient Involvement Using the Guidance for Reporting Involvement of Patients and the Public (version 2) Short Form Reporting Checklist[43]

Topic	Item	Section(s)
Aim	To better understand the benefits and challenges of living with a voice prothesis and the use of heat moisture exchangers from the perspective of those with lived experience as a Laryngectomee.	Key messages
Methods	In December 2024 following feedback from external interested parties regarding our initial draft report we reached out to patient groups to better understand and gather insights from Laryngectomee patients living with voice prothesis and heat moisture exchangers. Three patients were identified through the Laryngectomee Association of British Columbia and accepted invitations to share their experiences. CDA-AMC Engagement staff offered all patients the opportunity to participate in a 30-minute introductory call to learn more about the details and context of the project, which 1 accepted (held on 9th Jan 25). All 3 Laryngectomee patients were provided a	Methods

	set of questions. Two patients opted for a 1 hour Zoom call (Jan 25), 1 of the patients interviewed also provided their written responses to the questions in addition to the call. One patient provided their written answers via email only. CDA-AMC offers a $100 gift card to select retailers as a gesture of thanks to patient participants. All patient contributors engaged in this project provided their consent for participating and all identified that they wanted to be publicly acknowledged by name in the report.	
Results of Engagement	Speaking to the patients helped to highlight when and why a device might work (or not) in one context and not another (for example, in extreme cold or hot weather, or living in rural and remote locations). The patient partner input also provided insights into important outcomes (i.e. communication, independence, and social engagement) and challenges of using the device, highlighting how the benefits outweigh the device's limitations. It also helped to identify equity considerations, highlighting how the maintenance costs related to VP and HME as well as maintenance supplies was considered a barrier, particularly disadvantaging those with middle- or lower incomes.	Key messages, summary of finding
Discussion and Conclusions	The insights and experience provided by Laryngectomee patients was used to supplement the understanding of the impact of using a voice protheses and heat moisture exchangers following a Laryngectomy. This opportunity to directly engage with someone with experience allowed the authors of our report to better understand the subject and contextualize the limited clinical and cost-effectiveness findings from the literature to provide a comprehensive picture of the benefits and challenges of using VP and HME devices for patients following a laryngectomy. Having a Voice Prothesis and Health Moisture Exchangers for patients following a laryngectomy is critical to their ability to live a fulfilled life, communicate with friends and family, maintain their independence, and prevent lung infection. Whilst there are challenges with maintaining the devices and additional costs for the supplies needed, the benefits of these devices were seen to far outweigh these challenges.	Conclusion and implications
Reflections and Critical Perspective	The patient contributors were highly engaged in their participation with Canada's Drug Agency. Patient engagement occurred after the rapid review was complete, it did not influence the formulation of research questions or outcomes of interest, which may limit the relevance and applicability of the findings. All of the patients were supported by CDA-AMC Engagement Officers, and the interview was attended by 2 Engagement Officers. The introductory and engagement calls were scheduled at the patient's convenience, and the patients were sent the questions in advance so that they could prepare. A choice of honorarium or gift card was offered as a gesture of thanks for their time and expertise. One limitation was our method. While our virtual approach enabled participation from individuals across Canada, the need for patients to have reliable technology and internet access to participate in a Zoom or telephone call potentially excluded some voices. Another limitation in our method would be that all the participating patients live in the same province (British Columbia). We did reach out to patient groups across Canada however we only received a response from 1 patient group based in British Columbia that were already aware of the project and keen to provide their perspective.	Limitations

Appendix 6: The list of excluded studies

<excluded for single-arm primary study>

Heirman AN, Tellman RS, van der Molen L, et al. The acceptance and voice quality of a new voice prosthesis 'Vega High performance' - a feasibility study. *Acta Otolaryngol.* 2023;143(8):721-729.

<excluded for the primary study already included by at least one systematic review>

Ebersole B, Moran K, Gou J, et al. Heat and moisture exchanger cassettes: results of a quality/safety initiative to reduce postoperative mucus plugging after total laryngectomy. *Head Neck*. 2020;42(9):2453-2459.

Mayo-Yanez M, Cabo-Varela I, Suanzes-Hernandez J, Calvo-Henriquez C, Chiesa-Estomba C, Herranz Gonzalez-Botas J. Use of double flange voice prosthesis for periprosthetic leakage in laryngectomised patients: a prospective case-crossover study. *Clin Otolaryngol.* 2020;45(3):389-393.

Petersen JF, Lansaat L, Timmermans AJ, van der Noort V, Hilgers FJM, van den Brekel MWM. Postlaryngectomy prosthetic voice rehabilitation outcomes in a consecutive cohort of 232 patients over a 13-year period. *Head Neck*. 2019;41(3):623-631.

<Other publications>

Graville DJ, Palmer AD, Andersen PE, Cohen JI. Determining the efficacy and cost-effectiveness of the ActiValve: results of a long-term prospective trial. *Laryngoscope*. 2011;121(4):769-776.

Soolsma J, van den Brekel MW, Ackerstaff AH, Balm AJ, Tan B, Hilgers FJ. Long-term results of Provox ActiValve, solving the problem of frequent candida- and "underpressure"-related voice prosthesis replacements. *Laryngoscope*. 2008;118(2):252-257.

Retel VP, van den Boer C, Steuten LM, Okla S, Hilgers FJ, van den Brekel MW. Cost-effectiveness of heat and moisture exchangers compared to usual care for pulmonary rehabilitation after total laryngectomy in Poland. *Eur Arch Otorhinolaryngol*. 2015;272(9):2381-2388.

van Sluis KE, van der Molen L, van Son R, Hilgers FJM, Bhairosing PA, van den Brekel MWM. Objective and subjective voice outcomes after total laryngectomy: a systematic review. *Eur Arch Otorhinolaryngol*. 2018;275(1):11-26.

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