ORIGINAL ARTICLE

Evaluating the cost-effectiveness of laryngeal examination after elective total thyroidectomy

Running head: Routine examination is not cost-effective

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SYNOPSIS

Routine laryngeal examination after total thyroidectomy is not cost-effective against selective laryngeal examination done at 2-week, 1-month or 3-month after surgery. Selective laryngeal examination done at 3-month appears to be a reasonable selective strategy given its lowest overall cost.

ABSTRACT

Background

Although routine laryngeal examination (RLE) after thyroidectomy may cost more than selective laryngeal examination (SLE), it permits earlier detection and treatment of vocal cord palsy (VCP) and so may be cost-saving in the longer term. We compared the 2-year cost-effectiveness between RLE, SLE with LE done at 2 weeks (SLE-2w), 1-month (SLE-1m) and 3-month (SLE-3m) after thyroidectomy in the institution's perspective.

Methods

Our case definition was a hypothetical 50 year-old female who underwent an elective total thyroidectomy for a benign multinodular goiter. A decision-analytic modelling was constructed to compare the estimated cost-effectiveness between RLE, SLE-2w, SLE-1m and SLE-3m after a 2-year period. Outcome probabilities, utilities and costs were estimated from the literature. The threshold for cost-effectiveness was set at USD50,000/quality-adjusted life year (QALY). Sensitivity and threshold analyses were used to examine model uncertainty.

Results

RLE was not cost-effective because its incremental cost-effectiveness ratio to SLE-2w, SLE-1m and SLE-3m were USD302755, USD227883 and USD247105, respectively. RLE was only cost-effective when temporary VCP rate increased >42.7% or cost of LE equaled zero. Similarly, SLE-2w was only cost-effective to SLE-3m when dysphonia for temporary VCP at 3-month increased >39.13%, dysphonia for permanent VCP at 3-month increased >50.29% or dysphonia without VCP at 3-month increased >42.69%. However, none of these scenarios appeared clinically likely.

Conclusions

In the institution's perspective, RLE was not cost-effective against the other 3 SLE strategies. Regarding to the optimal timing of SLE, SLE-3m appears to be a reasonable and acceptable strategy because of its relative low overall cost.

INTRODUCTION

Thyroidectomy is one of the most commonly-performed surgical procedures and because postoperative vocal cord paresis or palsy (VCP) is an important procedural-related complication, information on the patient's postoperative vocal cord status is essential [1-4]. However, postoperative routine laryngeal examination (RLE) of the vocal cords (VC) remains controversial [1-4]. Although most surgeons would perform selective laryngeal examination (SLE) (i.e. laryngeal examination (LE) when voice symptoms/dysphonia have become persistent for some time after thyroidectomy), some prefer RLE [5-8]. A recent large audit has found the frequency of postoperative LE ranges between 0 to 100% [8].

One reason for such divided practice is the issue of cost-effectiveness in RLE as this has never been demonstrated [1-4]. Although RLE would cost more than SLE because more LE are done, recent studies have found that RLE permits earlier diagnosis and treatment of VCP (such as injection thyroplasty) (IT) and so may be cost-saving in the longer term [9-12]. Furthermore, unlike SLE, RLE greatly shortens the duration of dysphonia minimizing the loss of patient quality of life (QOL) (i.e. more effective) [9,13]. Therefore, RLE may prove more cost-effective than SLE in the longer term. The other issue is related to the timing of the SLE strategy as this could range between 2 weeks to 3 months from thyroidectomy [1-4,9]. Although an early LE would lead to an earlier diagnosis and treatment of VCP, it may increase the detection and treatment of VCP which are mostly temporary and fully recoverable without treatment [5,14]. Based on these arguments, a decision-tree analysis model was constructed to examine whether RLE was cost-effective to SLE over a medium term and also to find out the optimal cost-effective timing for the SLE strategy.

MATERIALS AND METHODS

A decision tree model using TreeAge Software Pro version 2013 (Treeage Software, Inc., Williamstown, MA, US) was constructed to compare the 2-year estimated cost-effectiveness between two main strategies, namely RLE and SLE after elective total thyroidectomy. Under the RLE strategy, all postoperative patients were subjected to LE within 1-2 days after operation. This was regardless of their voice quality or symptoms. As a result, the cause of dysphonia was made early and that led to early IT (for those with dysphonia and VCP) or speech therapy (for those with dysphonia but no VCP). In contrast, under the SLE strategy, only a select group of patients with persistent voice complaints or dysphonia for a period of time would undergo LE. As a result, the cause of dysphonia was not made until LE was performed after a period of dysphonia and that varied between 2 weeks to 3 months [1-4,9]. Since dysphonia rate and temporary VCP would decrease over time, the SLE was further divided into 3 sub-strategies to account for these time-related changes. They were SLE at 2-week (SLE-2w), at 1-month (SLE-1m), and at 3-month (SLE-3m) after thyroidectomy. Therefore, our model comprised four strategies, namely RLE, SLE-2w, SLE-1m, and SLE-3m. Figure 1 outlines the decision-analytic modelling.

Base-case patient

A 50 year-old female patient underwent an elective total thyroidectomy for a moderately enlarged but non-retrosternal benign multinodular goiter. She did not have any preoperative voice symptoms or VCP. Also she did not have any previous head and neck surgery or irradiation. Both recurrent laryngeal nerves (RLN) were clearly visualized and appeared intact at the end of thyroidectomy.

Data sources

Estimates of temporary and permanent VCP after total thyroidectomy were derived from pooling results of a recent systematic review and two recent large thyroid surgery registries [8,15,16]. The total number of patients pooled was 47,564. VCP rates were calculated based on number of patients rather than nerves-at-risk. Other probabilities of outcomes such as rates of postoperative dysphonia with and without VCP, recovery rate of temporary VCP and chance of permanent vocal cord medialization with and without IT at 2-week, 1-month, and 3-month were derived from a comprehensive PubMed search using free text search terms in 'All fields'. These search terms included 'dysphonia', 'vocal cord palsy', 'injection thyroplasty' and 'vocal cord medialization'. There was no language restriction or methodological filters. The bibliography of a recent clinical practice guideline on voice outcomes after surgery was also searched for additional relevant references [9]. Critical appraisal of each study was performed by 2 authors (BHL,CKW). Expert opinion was sought from 2 specialist otolaryngologists (RYT,BYW) if the outcome probabilities were not available in the literature. The range obtained from the experts was used to guide the sensitivity analysis if it was a more reliable source of information. Base-case values were derived by pooling the results of all retrieved studies. If only one study was available, the mid-point of the reported range was taken. Table 1a summarizes outcome probabilities.

Utilities

Effectiveness was measured by quality-adjusted life years (QALYs) gained. QALY adjusts the life-expectancy through the multiplication of QOL adjustment with duration stayed at each health state. The QOL adjustment is quantified by a utility score that typically ranges from 0 (death) to 1 (full health). Table 1b lists the utility score for each health state. In the present study, utilities were used as weights to calculate quality-adjusted life expectancy. A utility of 1.0 was assigned for a patient that underwent elective total thyroidectomy without dysphonia while 0.81 was assigned to any health state with the outcome of "dysphonia" after thyroidectomy regardless of cause [13].

Study design and decision models

The analysis was designed from an institution's perspective, using QALYs as the overall outcome measure. For each strategy, QALYs was the sum of two components, namely the time period stayed in full health (i.e. without dysphonia) multiplied by 1.0 and the time of dysphonia multiplied by the utility score of 0.81 within a 2-year period.

Cost data

Our model only looked at the cost of four strategies (i.e. RLE, SLE-2w, SLE-1m, and SLE-3m) from an institution's perspective. Total cost included procedural cost and complication cost. Indirect costs such as loss of productivity and wages were not included. Unit costs of LE, speech therapy, office-based IT and VC medialization under general anesthesia were estimated based on Medicare reimbursement for surgical procedure obtained from public access file from Centers for Medicare and Medicaid Services [17-19] and data obtained from previous cost-effectiveness analysis [20]. Table 1c summarizes the unit costs.

Assumptions

All LE were performed by expert otolaryngologists using standard technique without complications or discomfort. All VCP were assumed unilateral only because bilateral would not have been clinically silent. Patients with asymptomatic VCP were assumed to have a utility score of 1 (i.e. the state of a healthy individual without VCP). For patients with symptomatic VCP confirmed on LE, IT was given immediately without delay while those with dysphonia without VCP were given speech therapy. One single IT was assumed adequate for complete voice recovery in symptomatic VCP. ML was performed for permanent VCP 12 months after thyroidectomy.

Base-case analysis

This was done according to the established guideline for cost-effectiveness analysis [21]. The incremental cost-effectiveness ratio (ICER) was the only outcome measurement and equaled to [cost of strategy A – cost of strategy B] / [QALYs of strategy A – QALYs of strategy B]. A strategy was "cost-saving" if it was costing less and also more effective over the competing strategy (i.e. that strategy dominated the competing strategy). A strategy was regarded cost-effective over another strategy if the ICER was < USD50,000 per QALY gained. This threshold was chosen based on analysis of the cost of current healthcare resource allocation decisions in the US [22]. A strategy was regarded as "extended dominance" if it was less effective and had a higher ICER than one of the competing strategies.

Sensitivity analysis

Univariate sensitivity analysis was performed to evaluate the impact of various outcome probabilities on the base-case analysis. Strategies that had extended dominance in the base-case analysis were eliminated from the sensitivity analysis. Each clinical parameter varied from the lowest to the highest values as suggested in the literature while other parameters remained constant. Since RLE would cost more than SLE, a negative incremental effectiveness meant SLE was dominant. A threshold analysis was undertaken to capture the threshold clinical values at which the ICER of RLE relative to SLE became zero (cost equivalence favoring the RLE) or less than USD50,000 per QALY gained (RLE was cost-effective relative to SLE). The range of threshold analysis was considerably expanded by adopting the theoretical range from 0 to 100%.

RESULTS

Base-case analysis

Table 2 shows the results of base-case analysis. After a 2-year period, each patient in RLE spent an extra USD110.20 but gained an additional 0.00036 QALY over SLE-2w. Therefore, the RLE was more costly but also more effective than SLE-2w in the institution's perspective. However, since the ICER of USD302755 for RLE relative to SLE-2w was far above the recommended threshold, RLE was not more cost-effective than SLE-2w. RLE was also not cost-effective to the other 2 SLE sub-strategies as the ICER of RLE relative to SLE-1m, and SLE-3m were USD227883 and USD247105, respectively. By definition, SLE-1m was regarded as extended dominance because it was less effective than SLE-2w, and had a higher ICER ($364,022/QALY vs $161,994/QALY) than SLE-2w when comparing with SLE-3m. Therefore, SLE-1m was excluded from subsequent sensitivity analyses.

Sensitivity analysis

Table 3 shows the univariate sensitivity analysis of RLE vs. SLE-2w and SLE-2w vs. SLE-3m. Regarding to the comparison between RLE and SLE-2w, RLE remained not cost-effective to SLE-2w when key clinical parameters such as rates of VCP, dysphonia and permanent ML after IT were varied. Varying these parameters still yielded positive ICERs well above the threshold of 50,000 implying RLE was not cost-effective. RLE only became cost-saving to SLE-2w if the cost of LE became zero. For the comparison between SLE-2w and SLE-3m, SLE-2w became cost-effective to SLE-3m if rates of permanent VCP increased to 18.6%, dysphonia either in temporary or permanent VCP at 3-month increased to 80.6%, or dysphonia without VCP at 3-month increased to 87.0%. However, since the permanent VCP rate could not rise above the temporary VCP rate, this was excluded from the subsequent threshold analysis.

Table 4 shows the threshold analyses of RLE vs. SLE-2w and SLE-2w vs. SLE-3m. RLE became cost-effective to SLE-2w if temporary VCP after total thyroidectomy increased from 7.12% to 42.74% (i.e. around 6 times) (see appendix 1). SLE-2w became cost-effective to SLE-3m if dysphonia in temporary VCP at 3-month increased > 39.13% (see appendix 2). Other scenarios included dysphonia in permanent VCP at 3-month increased >50.29% and dysphonia without VCP at 3-month increased >42.69%.

DISCUSSION

Given the controversies with RLE, the present study is the first ever attempt at evaluating whether RLE could be cost-effective relative to the three different SLE strategies based on timing of LE. In terms of cost per person, RLE was unsurprisingly the most costly strategy against the other strategies. Relative to the lowest cost strategy (SLE-3m), RLE cost 5.8 times more. This was because under the RLE strategy, more patients were subjected to postoperative LE whereas under the SLE-3m strategy, only those with persistent dysphonia for 3 months were subjected to postoperative LE. In fact, there was a gradual decrease in cost per person as the timing of SLE became delayed (from 2-week to 3-month). This was because fewer LE were required over time as the rate of dysphonia decreased over time. In addition, since most VCPs were temporary (i.e. neurapraxia) and tended to recover spontaneously (without treatment), the actual number of VCP detected and required IT under the SLE-3m strategy were among the lowest. In fact, by 2 months, more than 60% of temporary VCP would have recovered without any treatment or intervention [14]. Although the chance of having more expensive VC medialization in delayed LE might be higher because of delayed diagnosis and treatment of VCP, our data showed that this did not greatly increase the overall cost as suggested by previous studies [9-12].

In terms of effectiveness, RLE was also the most effective strategy because all VCP and dysphonia would have been diagnosed and managed within days after thyroidectomy whereas under the three SLE strategies, there was gradual loss of QOL over time because patients suffered longer duration of dysphonia and lower chance of normal voice recovery. However, despite being the most effective strategy based on these arguments, RLE was not cost-effective to SLE-2w, SLE-1m and SLE-3m.

Both the sensitivity and threshold analyses of RLE vs. SLE-2w showed that almost none of the reported ranges in clinical parameters affected our conclusion unless the cost of LE was reduced to zero or temporary VCP increased significantly to 42.7% (i.e. 6 times higher than the reported rate). In contrast, the threshold analysis of SLE-2w vs. SLE-3m did find three possible scenarios which were within the reported ranges and could potentially make SLE-2w cost-effective to SLE-3m. However, they were probably clinically unlikely because it is unusual to have such high percentage of postoperative patients complaining of persistent dysphonia 3 months after surgery irrespective of the cause of dysphonia [23-28].

Therefore, RLE was not cost-effective against the other 3 SLE strategies. Relative to the other 2 SLE strategies, SLE-3m appears a more reasonable and acceptable strategy because of its low cost.

However, despite these results, we do acknowledge several shortcomings. Firstly, our model did not account for potential benefits of self-auditing in RLE (i.e. the surgeon could learn his/her own RLN injury rates and improve) [1,2]. Although this may not affect the present injury rates, it would reduce future injuries and so in the longer term, RLE may prove cost-effective relative to SLE strategies. Secondly, some of the assumptions might have been over-simplified. For example, patients with asymptomatic VCP do not necessarily have a normal health state (utility score of 1.0) as subtle changes affecting QOL loss are possible. Also it is arguable whether every patient with VCP/dysphonia requires immediate IT. Close observation might be more appropriate in mild dysphonia. In actual practice, VCP could be bilateral and 2-3 thyroplasties are often required to manage severely symptomatic VCP [10-12]. Also the latter is not necessarily free of complications/discomfort. Nevertheless, most of these would only have increased the ICER of RLE relative to SLE strategies. Also, some of the newer developments (e.g. laryngeal electromyography) in characterizing severity and prognosis of VCP were not included and despite a comprehensive literature search, selection and publication biases could not be completely ruled out as none of the studies examined were randomized studies.

CONCLUSION

RLE could not be recommended based on cost-effectiveness unless temporary VCP rate increased by 6 times or cost of LE was reduced to zero. Regarding to the optimal timing for SLE strategy, SLE-2w could only become cost-effective to SLE-3m if dysphonia necessitating LE remained very high (>40%) at 3-month. Therefore, in the institution's perspective, RLE was not cost-effective against the other 3 SLE strategies. Relative to the other 2 SLE strategies, SLE-3m appears a more reasonable strategy given its relative low overall cost.

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Table 1a. Literature-based probabilities

Clinical Parameters	**Base case (%)**	**Range for sensitivity analysis (%)**	**Reference**
Unilateral vocal cord palsy after total thyroidectomy (%)			
- Temporary	7.1	1.4 – 38.4	8,15,16
- Permanent	2.0	0.0 – 18.6	8,15,16
Dysphonia rate in the presence of temporary or permanent unilateral vocal cord palsy (%)			
- at 2-week	50.5	20.4 – 80.6	9,29,experts
- at 1-month	40.5	20.4 – 80.6	9,29,experts
- at 2-month	30.5	20.4 – 80.6	9,29,experts
- at 3-month	20.5	20.4 – 80.6	9,29,experts
Dysphonia rate without vocal cord palsy (%)			
- at 2- week	44.1	14.0 – 87.0	23-28,30,31,experts
- at 1-month	34.1	14.0 – 87.0	23-28,30,31,experts
- at 2-month	24.1	14.0 – 87.0	23-28,30,31,experts
- at 3-month	14.1	14.0 – 87.0	23-28,30,31,experts
Recovery rate for temporary vocal cord palsy (%)			
- at 2-week	29.6	29.6	14
- at 1-month	46.1	46.1	14
- at 2-month	62.5	62.5	14
- at 3-month	68.8	68.8	14

Rate of permanent vocal cord medialization based on the delay from injury to first injection thyroplasty (%)			
- 2 week to < 1 month	0	0.00 – 26.3	10-12
- 1 month to < 2 month	20.0	20.0 – 26.3	10-12
- 2 month to < 3 month	33.3	26.3 – 37.5	10-12
- 3 month to < 4 month	33.3	26.3 – 37.5	10-12

Table 1b. Utility score for each health state in model

Health state in model	**Utility Score**	**Reference**
Post-thyroidectomy patients		
-no dysphonia	1.00	13
-dysphonia	0.81	13

Table 1c. Unit cost (USD) for each service component for post-thyroidectomy

Cost component	**Unit cost in USD**	**Reference**
Laryngeal examination of the vocal cords	115.52	17-19
Speech therapy	102.6	17-19
Injection laryngoplasty under local anesthesia (office-based)	496.00	17-19
Permanent vocal cord medialization under general anesthesia	4511.80	17-19

Table 2. Cost (USD) and quality-adjusted life expectancy (QALYs) per person for each laryngeal examination strategy, and the incremental cost-effective ratio (ICER) (USD/QALYs) of a laryngeal examination strategy compared with other competing strategies after elective total thyroidectomy.

	Laryngeal examination strategies*			
	Routine laryngeal examination	Selective laryngeal examination at 2-week	Selective laryngeal examination at 1-month	Selective laryngeal examination at 3-month
Cost (USD) per person	179.471	69.268	61.655	30.714
Incremental cost compared with routine laryngeal examination	-	110.203	117.816	148.757
Expected QALYs per person	2.000	1.99964	1.99948	1.99940
Incremental QALYs/100,000 persons compared with routine laryngeal examination	-	36	52	60
	Competing Laryngeal examination strategy			
ICER (cost/QALYs)	Routine laryngeal examination	Selective laryngeal examination at 2-week	Selective laryngeal examination at 1-month	Selective laryngeal examination at 3-month
Routine laryngeal examination	-	302755	227883	247105

Selective laryngeal examination at 2-week	-	-	Extended dominance	161994
Selective laryngeal examination at 1-month	-	-	-	364022

*Sort by descending order of QALYs

Table 3. Sensitivity analysis between routine laryngeal examination (RLE), selective laryngeal examination at 2-week (SLE-2w) and at 3-month (SLE-3m) after thyroidectomy.

		RLE vs. SLE-2w					***SLE-2w vs. SLE-3m***			
Clinical Parameters	Parameter Range (%)	Incremental QALYs/100,000 persons		Range for ICER			Incremental QALYs/100,000 persons		Range for ICER	
Unilateral vocal cord palsy after total thyroidectomy (%)										
- Temporary VCP	1.4 – 38.4	14	161	836877.75	56941.82		14	78	215002.98	110603.74
- Permanent VCP	0.0 – 18.6	28	103	391219.23	97751.28		12	119	337303.45	10714.22
Dysphonia rate in the presence of temporary unilateral vocal cord palsy (%)										
- at 2-week	20.4 – 80.6	19	53	633351.00	181817.30		41	7	62438.57	757128.30
- at 3-month	20.4 – 80.6	36	36	302452.87	302452.87		24	143	163611.87	8634.37
Dysphonia rate in the presence of permanent unilateral vocal cord palsy (%)										
- at 2-week	20.4 – 80.6	32	41	359378.25	258658.92		29	19	122228.76	221766.07
- at 3-month	20.4 – 80.6	36	36	302452.87	302452.87		24	81	162885.09	16389.93
Dysphonia rate without vocal cord palsy (%)										
- at 2-week	14.0 – 87.0	36	36	379485.55	192662.10		24	24	44079.14	330211.18
- at 3-month	14.0 – 87.0	36	36	302452.87	302452.87		24	24	162451.57	Favoring SLE-2w
Rate of permanent vocal cord medialization based on the delay from injury to first injection thyroplasty (%)										
- 2 week to < 1 month	0.00 – 26.3	36	36	302452.87	269666.93		24	24	162059.61	212273.37

- 3 month to < 4 month	26.3 – 37.5	36	36	302452.87	302452.87		24	24	167484.96	158804.41
Cost component										
Laryngeal examination	0 – 1000	36	36	Favoring RLE	2618186.18		24	24	148783.23	263710.38
Speech therapy	0 – 1000	36	36	302452.87	302452.87		24	24	44471.10	1190557.96
Injection laryngoplasty under local anesthesia (office-based)	0 – 1000	36	36	302452.87	302452.87		24	24	105055.75	219982.90
Permanent cord medialization under general anesthesia	0 – 1000	36	36	302452.87	302452.87		24	24	187868.76	182148.39

Abbreviations: QALYs = Quality-adjusted life-years; ICER = Incremental cost-effectiveness ratio

Table 4. Threshold analysis of values at which routine laryngeal examination (RLE) became cost-effective to selective laryngeal examination at 2-week (SLE-2w) or SLE-2w became cost-effective to selective laryngeal examination at 3-month (SLE-3m)

RLE vs. SLE-2w						
Clinical Parameters	Base-case (%)	Threshold values at ICER=50,000	Values at ICER>50,000	Values at ICER between 0 and 50,000	RLE became cost-saving	RLE became cost-saving
Unilateral vocal cord palsy after total thyroidectomy	7.120	42.741	0.000-42.741	42.741-100.000	NA	NA
SLE-2w vs. SLE-3m						
Clinical Parameters	Base-case (%)	Threshold values at ICER=50,000	Values at ICER>50,000	Values at ICER between 0 and 50,000	SLE-2w became cost-saving	SLE-2w became cost-saving
Dysphonia rate in temporary vocal cord palsy (%)						
- at 3-month	20.5	39.131	8.551-39.131	39.131-100.000	NA	0.000-8.551
Dysphonia rate in permanent vocal cord palsy (%)						
- at 3-month	20.5	50.291	0.000-50.291	50.291-100.000	NA	NA
Dysphonia rate without vocal cord palsy (%)						
- at 3-month	14.1	42.689	0.000-42.689	42.689-55.446	55.446-100.000	NA

LEGENDS

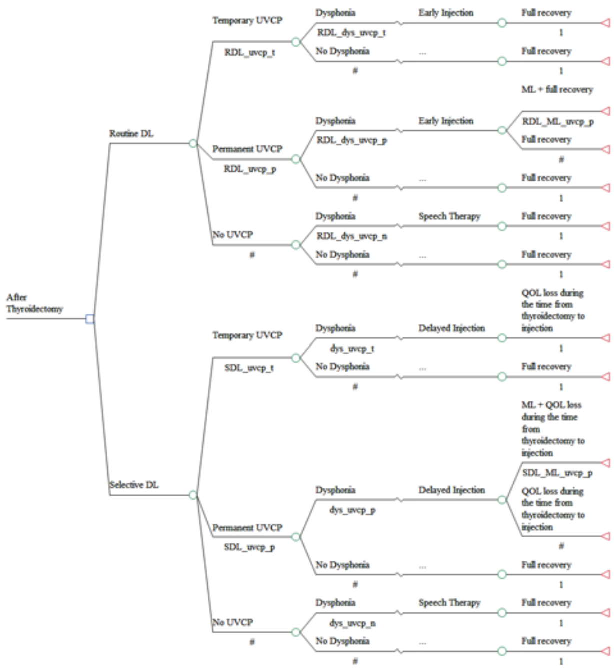
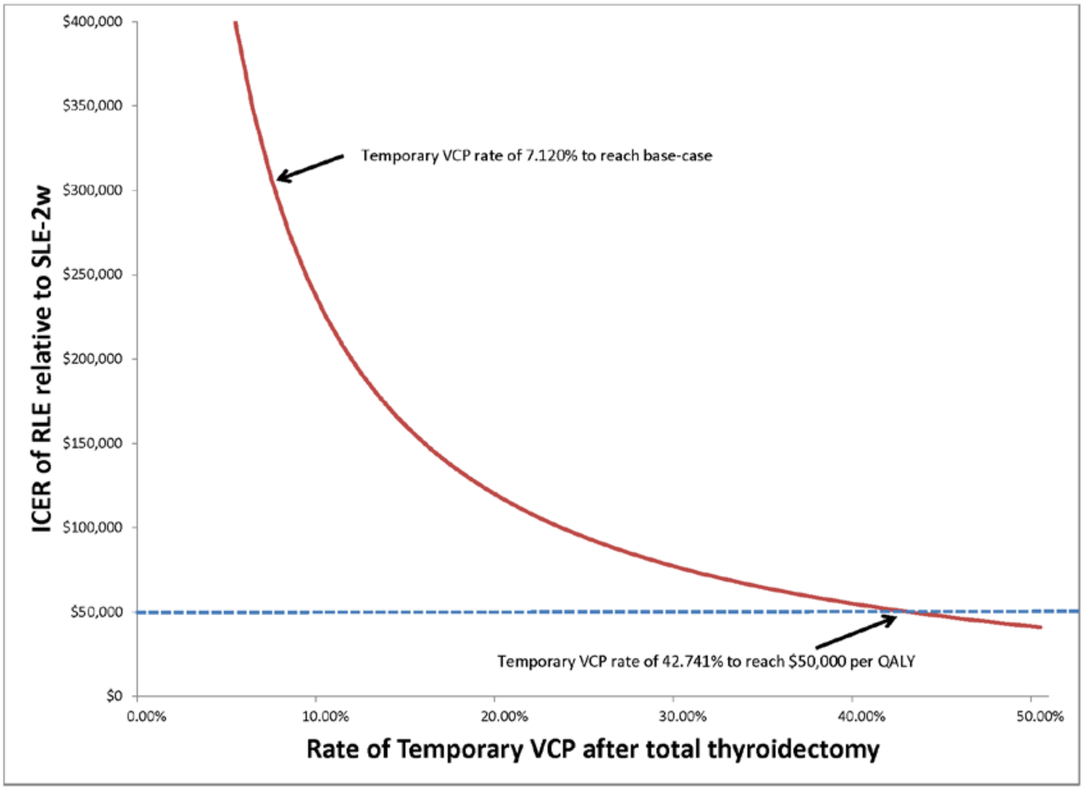
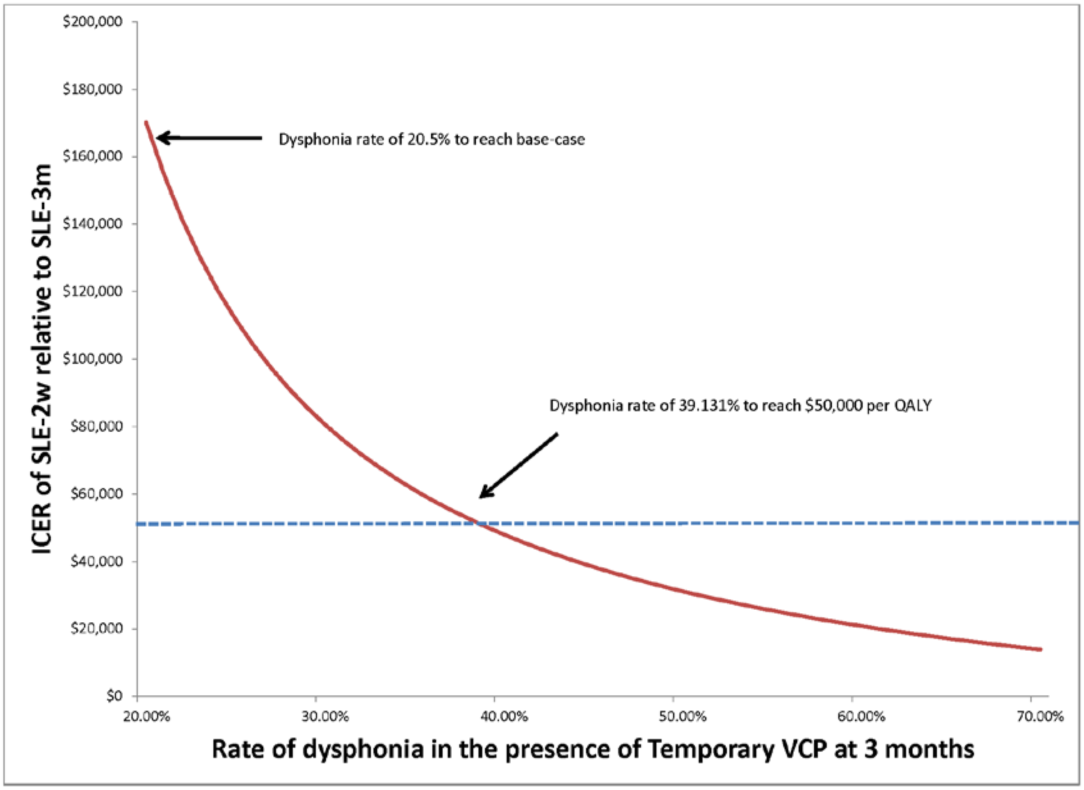


Figure 1. The decision-analytic modelling.



Appendix 1. One way-sensitivity analysis of the incremental cost-effectiveness ratio (ICER) of routine laryngeal examination (RLE) over selective laryngeal examination at 2-week (SLE-2w) as a function of rate of temporary vocal cord palsy after total thyroidectomy. The dashed line represents the 50,000/QALY threshold for cost-effectiveness.



Appendix 2. One way-sensitivity analysis of the incremental cost-effectiveness ratio (ICER) of selective laryngeal examination at 2-week (SLE-2w) over SLE at 3-month (SLE-3m) as a function of dysphonia in the presence of temporary vocal cord palsy at 3-month after total thyroidectomy. The dashed line represents the 50,000/QALY threshold for cost-effectiveness.