Title	A Cost-Minimization Analysis Comparing Total Thyroidectomy Alone and Total Thyroidectomy with Prophylactic Central Neck Dissection in Clinically Nodal-Negative Papillary Thyroid Carcinoma
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ORIGINAL ARTICLE

A cost-minimization analysis comparing total thyroidectomy alone and total thyroidectomy with prophylactic central neck dissection in clinically nodal negative papillary thyroid carcinoma

Running head: TT+pCND costs significantly more than TT alone

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SYNOPSIS

The addition of prophylactic central neck dissection at the time of total thyroidectomy in clinically-nodal negative papillary thyroid carcinoma was not cost saving in the medium to long term because of the initial higher cost and relatively small reduction in recurrence and need for reoperation.

ABSTRACT

Background: Total thyroidectomy (TT) with prophylactic central neck dissection (pCND) remains controversial for clinically-nodal negative (cN0) papillary thyroid carcinoma (PTC) and the issue of cost has rarely been examined. We aimed to evaluate whether pCND at the time of TT is more cost-saving than TT alone in the medium to long-term.

Methods: For a hypothetical group of 50 years old females with a 1.5cm cN0 PTC, a decision-tree model using TreeAge Software was developed to simulate outcomes and compare the 20-year accumulative direct cost between TT alone and TT+pCND strategies. Baseline values and ranges were determined from a systematic review of the literature. Sensitivity analyses were conducted to test model strength. Cost estimate of surgical procedures, complications and radioiodine (RAI) ablation was based on government gazette.

Results: The cost accrued per patient in the primary operation under TT alone and TT+pCND strategies were USD 6702.81 and USD 10062.35, respectively while the cost in the reoperative procedure were USD 12981.40 and USD 12509.09, respectively. The 20-year accumulative cost for TT alone and TT+pCND strategies were USD 19888.36 and USD 22760.86, respectively. The incremental cost per patient was USD 2872.50. In the univariate and bivariate sensitivity analyses, no change in conclusion was seen by varying the rates of complications, annualized locoregional recurrences and RAI or by extending the model to 50 years.

Conclusions

From a pure economic institution's perspective, TT+pCND is more expensive in the medium and long terms and seems less justified over TT alone in cN0 PTC.

INTRODUCTION

Papillary thyroid carcinoma (PTC) is the most common type of thyroid carcinoma with its incidence doubled over the last two decades.[1-5] However, despite good prognosis, locoregional recurrence (LRR) is common after curative surgery.[6] With recognition of the step-wise progression of metastasis from central (level VI) to lateral compartments (levels II-V), routine prophylactic central neck dissection (pCND) has been advocated at the time of total thyroidectomy (TT) to reduce LRR.[7-9] Although formal central neck dissection is indicated in clinically positive nodal disease, it remains controversial in clinically negative nodal disease (cN0).[10] There is little evidence to suggest patients with cN0 PTC would benefit from pCND at the time of TT, although a recently meta-analysis has found a 35% reduction in LRR over TT alone.[11] However, this was at the expense of higher risks of temporary hypoparathyroidism and overall morbidity.[11] Therefore, performing pCND may cause initial higher patient morbidity but may be beneficial in the medium to long-term because of reduced LRR.[9,11]

Despite this ongoing debate on whether routine pCND should or should not be performed, the issue of cost has rarely been discussed and examined. In the era of cost containment and rising healthcare costs, it is imperative that clinicians include dollar cost of a surgical intervention (such as pCND) as part of their decision making process. In the context of pCND for cN0 PTC, the question is whether the higher expected initial cost (due to greater extent of surgery, higher morbidity and more frequent radioiodine (RAI) use) could be compensated in the medium to long term by the lower cost from reduced LRR and need for reoperation.[11-14] We used a decision-tree analysis model to compare the medium to long-term cost between the two strategies, namely TT alone and TT+pCND in a reference population with biopsy-proven cN0 PTC.

MATERIALS AND METHODS

Case definition

A hypothetical cohort of 100,000 non-pregnant female patients aged 50 year-old with an unifocal intrathyroidal 1.5cm cN0 PTC in the right thyroid lobe and with no previous thyroidectomy or neck irradiation was simulated in the model.

The model

A decision tree model using TreeAge Software Pro version 2012 (Treeage Software, Inc., Williamstown, MA, US) was constructed to compare the estimated long-term cost between TT alone and TT+pCND. Patients were entered into the model after primary operation as the initial state, based on the Markov process with 1-year cycle as outlined in Figure 1. Patients underwent one of two strategies, namely TT alone or TT+pCND, and were followed up until 70 years old. The model included 3 major health states after primary treatment and they were disease-free, surveillance with LRR and death. In case of LRR involving either the central, lateral or central and lateral compartments, a compartment-oriented reoperation followed by RAI were offered. Patient in either two strategies may suffer one of six surgical complications from the primary operation. Patients were followed up until stage of death or 70 years old.

Assumptions

It was assumed all pCNDs were unilateral only and surgical resection was the only option in patients with LRR involving the central, lateral or central and lateral compartments. All patients were assumed suitable and agreed for reoperation at the time of LRR. For simplicity, only a maximum of one LRR and one reoperation per patient was assumed. Similarly, only one surgical complication was encountered after primary operation and reoperation. Reoperative CND was assumed bilateral while reoperative lateral SND was assumed unilateral involving levels II-V. An empirical 3GBq RAI was given after each reoperation. The costs of preoperative assessment and surveillance were assumed the same in both groups. Full compliance was assumed for all kinds of assessment, treatment and surveillance.

Probabilities

Estimates of the complications arising from the primary operation, postoperative radioiodine ablation (RAI) and central and/or lateral recurrences after primary operation were based a comprehensive literature search but were limited to those studies which directly compared surgical complications between TT alone and TT+pCND in cN0 PTC. Details of the search had been previously described.[11] Estimates of the complications arising from reoperation and death from non-thyroid causes were based on separate PubMed literature searches. To come up with an estimate for all clinical parameters, base-case values were derived from multiple studies synthesized in literature search. We tested the possible range of the lowest and highest values from aforementioned studies in the sensitivity analysis. The annual mortality rate of female patients in quinqueenial age groups (e.g. 50-54, 55-59, etc) were obtained from the population projection in 2012.[15]

Cost data

This model looked at the financial impact of two strategies from the institutional perspective. The cost from the institutional perspective only included the direct costs of the procedure, its associated complications, hospitalization. Indirect costs such as loss of productivity and wages were not included. The unit cost of all surgical procedures, RAI and complications were based on the Hospital Authority (HA) cost published in the 2013 Government Gazette.[16] The Gazette provides the official price list of all medical services utilized in healthcare sector. The operation costs included preoperative work-up cost, fees for the surgeon, anesthetist and supporting staff, drugs related to the operation, operating room, consumables and all other general expenses. Costs related to prolonged hospitalization or readmission due to complications or medical co-morbidities were not included. Drug costs were retrieved from the drug price enquiry system.[17] Cost data evaluated in Hong Kong dollar (HKD) (year 2013 values) were converted to US dollars (USD) at an exchange rate of USD 1.0= HKD7.8 and rounded off to the nearest whole USD dollar. Therefore, all monetary values were expressed in USD for international comparisons.

Base-case analysis

The 20-year accumulative medical cost accrued per patient for two strategies was calculated. All the costs were discounted by an annual rate of 3%, in line with the established guideline for cost-analysis.[18] The incremental cost difference was defined as the cost of TT+pCND minus the cost of TT alone.

Sensitivity analysis

Our models performed the one-way (univariate) sensitivity analysis to explore the uncertainty on the clinical parameters of complications, RAI ablation, and annualized recurrence rates. Each clinical parameter was varied over the lowest and highest possible values suggested in the literature search while the value of other clinical parameters remained constant. Since the complication rates in primary operation differed, those complication rates from primary operation were assumed the same between the two strategies in bivariate sensitivity analysis. We also performed bivariate sensitivity analysis on the surgical complications in which we varied the relative differences in rate of permanent vocal cord palsy complication between TT+pCND and TT alone, so as to obtain the incremental cost equivalence. Threshold analysis was undertaken to capture the threshold clinical values at which the costs of TT alone and TT+pCND became equivalent. We expanded considerably more on the range of threshold analysis by adopting the theoretical possible range from zero to one.

RESULTS

Base-case analysis

The base-case analysis was based on the previously stated assumptions and used the base-case probabilities and costs from Table 1 and 2. The costs accrued per patient in the primary operation under the TT alone and TT+pCND strategies were USD 6702.81 and USD 10062.35, respectively and the costs accrued per patient in the reoperation under the TT alone and TT+pCND strategies were USD 12981.40 and USD 12509.09, respectively. Table 3 shows the results of base-case and sensitivity analyses. From the institutional perspective, the 20-year accumulative cost of TT alone accrued per patient was USD 19888.36 while the cost of TT+pCND accrued per patient was USD 22760.86. Therefore, TT alone was the less expensive than TT+pCND to the institution.

Sensitivity analysis

The univariate sensitivity analysis was performed by varying key model parameters to verify the robustness of model conclusion. No change in the conclusion was seen by varying various key parameters including rates of complications, annualized LRR and RAI after primary operation. Even when the model was extended to 50 years, TT alone was less expensive than TT+pCND. In the bivariate sensitivity analysis, when the total morbidity after the primary operation in TT+pCND was assumed to be equal to TT alone, TT+pCND remained more costly than TT alone. When the total morbidity of TT+pCND was reduced from 29.96% to 14.94% (i.e. total morbidity of TT alone), the incremental cost remained positive (USD 2870.29). In fact, regardless of the actual total morbidity rate, so long as the two strategies had similar morbidity, TT+pCND remained more expensive than TT alone.

Table 4 shows the threshold analysis. Of all the clinical key model parameters, only 5 parameters could have made the direct medical cost of TT alone ≥ TT+pCND. These 5 parameters were permanent vocal cord palsy rate during TT alone, the 3 annualized recurrence rates under the TT alone strategy and rate of RAI ablation after TT+pCND. For the first parameter, the rate of permanent vocal cord palsy during TT alone had to rise above 59.84% while the rate of permanent

vocal cord palsy during TT+pCND remained at 1.22% before TT alone could become more costly than TT+pCND. In that scenario, the total morbidity would have to become 73.76% in TT alone while TT+pCND remained at 29.96%. Increasing the rates of central, lateral and central and lateral recurrence in TT alone also resulted in a decrease in incremental costs. The annualized central recurrence rate in TT alone had to rise from 0.63% to 7.34% before TT alone became more expensive. Similarly, the annualized lateral and central and lateral recurrence rates in TT alone had to rise from 0.38% to 4.54% and 0.56% to 3.71%, respectively before TT alone would become more costly than TT+pCND. A decrease in RAI ablation from 76.87% to 1.67% in TT+pCND while maintaining the rate of RAI in TT alone at 53.44% also resulted in equivalent direct medical costs between the two strategies.

DISCUSSION

To our knowledge, the issue of costs has rarely been discussed in the context of pCND. Our key question was whether adding pCND at the time of TT in cN0 PTC would be cost saving in the medium to long term. Our initial hypothesis was that although the addition of pCND at the time of TT may accrue a higher initial cost, this extra cost may perhaps be recovered by the lower LRR and need for reoperation over time.[11-14] Our hypothesis was supported by the fact that the primary operation cost accrued per patient in the TT alone was less than TT+pCND (USD 6702.81 and USD 10062.35, respectively) while the reoperation cost accrued per patient in TT alone was more than TT+pCND (USD 12981.40 and USD 12509.09, respectively). However, despite these findings, TT+pCND turned out USD 2872.50 more expensive than TT alone over a 20-year period. Even when the model was extended to a 50-year period, the TT+pCND remained more expensive by USD 2737.52.

The factors which led to the higher initial cost in TT+pCND included extra cost of pCND, higher complication rates from the primary operation and higher frequent of RAI ablation after primary operation. Under our service cost structure, pCND cost USD 2494.0 and that accounted for a third of the total cost of TT+pCND (USD 7006) or >50% the cost of TT (USD 4512). Also because the overall initial complication rate was higher in TT+pCND than TT alone (29.96% vs. 14.94%), the initial cost of TT+pCND was higher than TT alone. Regarding RAI ablation, since patients who underwent pCND were more likely to be upstaged by metastatic central lymph nodes,[7-9,11,12] RAI ablation was given more frequently in the TT+pCND strategy.

Although the cost accrued per patient in the reoperation setting was higher in the TT alone strategy than TT+pCND strategy (i.e. consistent to our initial hypothesis), the actual cost difference over time was not enough to compensate for the initial cost difference. The incremental cost difference was only USD 472.31 whereas the incremental cost difference in the primary operation setting was USD 3359.54. However, this could be explained firstly because under our service cost structure, the cost of primary CND and reoperative CND was similar, even though reoperation required greater

surgical skills and longer procedural time.[13,14] Secondly, from the literature, the complication rates from reoperation were not significantly higher than those from the primary operation. Both temporary hypoparathyroidism (20.64% vs. 17.14%) and overall morbidity (29.96% vs. 30.40%) rate were not too dissimilar to reoperative CND. The other factor was the low absolute LRR in TT alone. Although the LRR in TT alone was higher than that in TT+pCND (1.57% vs. 1.07%), the absolute difference was small and that led to smaller incremental cost difference. In fact, based on the threshold analysis, the annualized LRR had to increase by > 6–12 times before the cost of the two strategies become equivalent at 20 years. Other clinical scenarios were when the permanent vocal cord palsy rate in TT alone rose to ≥60% while the rate in TT+pCND remained 1.7% or when the use of RAI ablation after TT+pCND was reduced from 76.87% to 1.67%.

Despite these findings, there were several shortcomings with our model. Firstly, our findings were based on our own unique service cost structure and so the actual costs may not be applicable to other health systems and countries. Secondly, despite a comprehensive literature search for estimating different probabilities, selection and publication biases could not be completely ruled out. For example, base-case temporary and permanent vocal cord palsy rates in TT+pCND were not significantly higher than the TT alone (3.28% vs. 3.10% and 1.70% vs. 1.22%, respectively). Nevertheless, according to the two-way sensitivity analysis, even if TT+pCND had the same overall morbidity as TT alone, TT alone remained the less costly strategy. Thirdly, some of the assumptions might have been overly simplified. For example, assuming one LRR and one reoperation per patient would appear overly-simplified because up to 10% of patients with first-time LRR would require more than one reoperations.[14,15] Given the higher LRR rate in the TT alone, including ≥2 reoperations could potentially increase the cost accrued in TT alone. In addition, although the literature would suggest that RAI is given more often after TT+pCND than TT alone because of tumor upstaging,[11,12] there is currently no evidence to suggest that it should. In fact, some would argue that if nodal status is unknown (such as those without pCND), RAI should be given routinely (i.e. more frequently) to facilitate long-term follow-up.

One point worth noting is that this study evaluated only the costs accrued from an institution's perspective and not from the surgeon's or patient's perspective. To the surgeon or patient, TT+pCND might still be more preferable because overall LRR risk was reduced by almost half (from 1.57% to 0.87%). Perhaps, future studies could also study the relative impact of primary operation and reoperation on patients' quality of life.

CONCLUSION

From an institution's perspective, the addition of pCND at the time of TT for cN0 PTC was not cost saving in the medium to long term. This was partly because of higher initial cost in TT+pCND and relatively small difference in LRR between TT alone and TT+pCND. From an institution's perspective, TT alone was a much less costly strategy than TT+pCND.

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None

COMPETING INTERESTS

The authors declare that they have no competing interests.

AUTHORS CONTRIBUTIONS

BHH Lang / CKH Wong were involved in the review of literature, acquisition of data and drafting and completing the manuscript. BHH Lang / CKH Wong was also involved in the review of literature and drafting the manuscript. BHH Lang / CKH Wong conceived the study, participated in the co-ordination and the acquisition of data and helped to draft the manuscript. All authors read and approved the final manuscript.

Table 1. Literature-based probabilities

Clinical Parameters	**Base case (%)**	**Range for sensitivity analysis (%)**	**References**
Complications from the primary operation			
- Temporary vocal cord palsy			
- Total thyroidectomy alone	3.10	0.00 – 6.38	8,9,20-28
- Total thyroidectomy + prophylactic CND	3.28	0.00 – 7.26	8,9,20-28
- Permanent vocal cord palsy			
- Total thyroidectomy alone	1.22	0.00 – 2.74	8,9,20,22-25,27,28
- Total thyroidectomy + prophylactic CND	1.70	0.0 – 2.51	8,9,20,22-25,27,28
- Temporary hypoparathyroidism			
- Total thyroidectomy alone	7.73	4.03 – 33.63	8,9,20-28
- Total thyroidectomy + prophylactic CND	20.64	8.70 – 42.86	8,9,20-28
- Permanent hypoparathyroidism			
- Total thyroidectomy alone	0.85	0.00 – 8.11	8,9,21-28
- Total thyroidectomy + prophylactic CND	1.47	0.0 – 5.88	8,9,21-28
- Hematoma formation requiring reoperation			
- Total thyroidectomy alone	0.99	0.00 – 3.08	8,9,20-22,24,25,27
- Total thyroidectomy + prophylactic CND	1.79	0.00 – 2.50	8,9,20-22,24,25,27
- Wound infection			
- Total thyroidectomy alone	1.07	0.0 – 1.54	8,9,20-22,24-26
- Total thyroidectomy + prophylactic CND	1.16	0.0 – 1.16	8,9,20-22,24-26
- Total morbidity*			

- Total thyroidectomy alone	14.94		
- Total thyroidectomy + prophylactic CND	29.96		
Complications from reoperative CND			
- Temporary vocal cord palsy	4.04	1.59 – 22.22	29-36
- Permanent vocal cord palsy	2.70	0.00 – 17.78	29-36
- Temporary hypoparathyroidism	17.14	6.06 – 42.22	29-36
- Permanent hypoparathyroidism	1.70	0.00 – 5.00	29-36
- Hematoma	1.10	0.00 – 4.35	29,30,31,33,35
- Wound infection	1.92	0.00 – 4.35	29,30,31,33,35
- Chyle leakage	1.80	0.00 – 2.22	29,33,35
- Total morbidity*	30.40		
Complications from lateral selective neck dissection			
- Chyle leakage	5.51	5.8 – 5.83	37-39
Annualized locoregional recurrence rate			
- Central compartment only			
- Total thyroidectomy alone	0.63	0.00 – 1.83	8,9,20-28
- Total thyroidectomy + prophylactic CND	0.22	0.00 – 0.82	8,9,20-28
- Lateral compartment only			
- Total thyroidectomy alone	0.38	0.00 – 3.73	8,9,20-28
- Total thyroidectomy + prophylactic CND	0.36	0.00 – 1.57	8,9,20-28
- Central and lateral compartments			
- Total thyroidectomy alone	0.56	0.00 – 1.87	8,9,20-28
- Total thyroidectomy + prophylactic CND	0.29	0.00 – 0.41	8,9,20-28

- Overall locoregional recurrence rate			
- Total thyroidectomy alone	1.57		
- Total thyroidectomy + prophylactic CND	0.87		
Likelihood of RAI after primary operation			
- Total thyroidectomy alone	53.44	28.01 – 100.00	8,9,21,24,25,27,28,40,41
- Total thyroidectomy + prophylactic CND	76.87	58.09 – 100.00	8,9,21,24,25,27,28,40,41
Number of deaths per 1000 population			16
-50 – 54	1.8		
-55 – 59	2.5		
-60 – 64	4.0		
-65 – 69	6.0		
-70 – 74	10.3		
-75 – 79	20.0		
-80 – 84	37.7		
-85+	93.8		

Abbreviations: CND = central neck dissection; RAI = radioiodine ablation

* total morbidity was the sum of all complications; patients with more than one complication were counted as one

Table 2. Unit cost (USD) for each service component for the care of papillary thyroid carcinoma patients

	Unit cost (USD)	**Reference**
Surgical procedure		
- Total thyroidectomy	4512	17
- Central neck dissection (initial or reoperative)	2494	17
- Lateral selective neck dissection (reoperative)	5219	17
RAI ablation - Specialist consult, blood tests (TSH, Tg, Anti-Tg abs), recombinant TSH injections, RAI (3.3 Gbq) ablation, hospital stay (2 nights), post-treatment whole body scan	3820	17,18
Complications from primary operation or reoperation		
Temporary vocal cord palsy+ - Otolaryngology consult, laryngoscopy, follow-up visit, speech therapy	1383	17
Permanent vocal cord palsy# - Otolaryngology consult, laryngoscopy, follow-up visit, speech therapy, vocal cord medialization	4951	17
Temporary hypoparathyroidism+ - Follow-up visits, blood tests, medications	416	17,18
Permanent hypoparathyroidism (annual cost)# - Follow-up visits, blood tests, medications	444	17,18
Chyle leak*	4250	17
Hematoma requiring neck re-exploration	2442	17
Wound infection	1300	17
Routine Surveillance (annual cost)	800	17

Abbreviations: RAI = radioiodine; TSH = thyroid stimulating hormone; Tg = thyroglobulin; Anti-Tg abs = anti-thyroglobulin auto-antibodies

+ assumed an average of 2-month duration

includes monthly visit for the first 6 months and then thereafter 6-monthly follow-up

* assumed to be managed successfully with conservative treatment

Table 3. Results of base-case and sensitivity analyses

	Average direct medical cost (in USD) accrued per patient		
Base-case analysis	**TT alone**	**TT+pCND**	**Incremental cost**
	19888.36	22760.86	2872.5
Univariate sensitivity analysis			
Clinical parameters	**Range for sensitivity analysis (%)**	**Range for incremental cost (USD) per patient**	
TT alone			
Complications from primary operation			
- Temporary vocal cord palsy	0.00 – 6.38	2917.87 to 2829.63	
- Permanent vocal cord palsy	0.00 – 2.74	2962.61 to 2826.95	
- Temporary hypoparathyroidism	4.03 – 33.63	2887.90 to 2764.76	
- Permanent hypoparathyroidism	0.00 – 8.11	2883.03 to 2782.56	
- Hematoma requiring reoperation	0.00 – 3.08	2896.68 to 2821.47	
- Wound infection	0.00 – 1.54	2886.41 to 2866.39	
Complications from reoperative CND			
- Temporary vocal cord palsy	1.59 – 22.22	2877.81 to 2833.15	
- Permanent vocal cord palsy	0.00 – 17.78	2893.43 to 2755.65	
- Temporary hypoparathyroidism	6.06 – 42.22	2879.72 to 2856.17	
- Permanent hypoparathyroidism	0.00 – 5.00	2883.97 to 2850.24	
- Hematoma requiring reoperation	0.00 – 4.35	2876.71 to 2860.08	
- Wound infection	0.00 – 4.35	2876.41 to 2867.56	
- Chyle leakage	0.00 – 2.22	2884.48 to 2869.71	
Complications from lateral SND			
- Chyle leakage	5.21 – 5.83	2873.14 to 2871.82	
Annualized LR recurrence rate			
- Recurrence in central compartment	0.00 to 1.83	2066.93 to 3366.04	
- Recurrence in lateral compartment	0.00 to 3.73	3292.55 to 126.10	
- Recurrence in central and lateral compartments	0.00 to 1.87	3710.80 to 1189.91	
RAI ablation after primary operation	28.01 to 100.00	3843.93 to 1093.91	

TT+pCND		
Complications from primary operation		
- Temporary vocal cord palsy	0.00 – 7.26	2856.05 to 2956.45
- Permanent vocal cord palsy	0.00 – 2.51	2831.91 to 2956.18
- Temporary hypoparathyroidism	8.70 – 42.86	2822.83 to 2964.94
- Permanent hypoparathyroidism	0.00 – 5.88	2857.75 to 2916.75
- Hematoma requiring reoperation	0.00 – 2.50	2828.79 to 2889.84
- Wound infection	0.00 – 1.16	2857.42 to 2872.50
Complications from reoperative CND		
- Temporary vocal cord palsy	1.59 – 22.22	2870.14 to 2890.07
- Permanent vocal cord palsy	0.00 – 17.78	2863.17 to 2924.65
- Temporary hypoparathyroidism	6.06 – 42.22	2869.28 to 2879.79
- Permanent hypoparathyroidism	0.00 – 5.00	2867.47 to 2882.27
- Hematoma requiring reoperation	0.00 – 4.35	2870.63 to 2878.05
- Wound infection	0.00 – 4.35	2870.76 to 2874.71
- Chyle leakage	0.00 – 2.22	2867.16 to 2873.75
Complications from lateral SND		
- Chyle leakage	5.21 – 5.83	2871.53 to 2873.55
Annualized LR recurrence rate		
- Recurrence in central compartment	0.00 to 0.82	2688.30 to 3341.36
- Recurrence in lateral compartment	0.00 to 1.57	2189.08 to 3953.84
- Recurrence in central and lateral compartments	0.00 to 0.41	2415.96 to 3055.06
RAI ablation after primary operation	58.09 to 100.00	2155.11 to 3756.07
Year cycle	20 to 50 years	2872.50 to 2737.52
Discount rate	0 to 3	2735.54 to 2872.50
Bivariate sensitivity Analysis	**Value (%)**	**Incremental cost (USD) per patient**
Assuming equivalent total morbidity in primary operation between TT alone and TT+pCND		
- Total Morbidity of TT+pCND	29.96	2868.82
- Total Morbidity of TT alone	14.94	2870.29

- Total Morbidity	0.00	2872.29

Abbreviations: TT = total thyroidectomy; pCND = prophylactic central neck dissection; SND = selective neck dissection; LR = locoregional; RAI = radioiodine

Table 4. Threshold analysis of clinical values at which the direct medical costs of total thyroidectomy (TT) alone and total thyroidectomy and prophylactic central neck dissection (TT+CND) became equivalent over a 20-year period

Clinical parameters	Base-case (%)	Threshold (%)	Values for incremental cost < 0
TT alone			
- Permanent vocal cord palsy at primary operation	1.22	59.84	59.84, 100.00
- Annual recurrence in central compartment	0.63	7.34	7.34, 100.00
- Annual recurrence in lateral compartment	0.38	4.54	4.55, 100.00
- Annual recurrence in central and lateral compartments	0.56	3.71	3.71, 100.00
TT+pCND			
- RAI ablation	76.87	1.67	0.00, 1.67

Abbreviations: TT = total thyroidectomy; pCND = prophylactic central neck dissection

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LEGENDS

Figure 1. A simplified tree diagram representing the decision tree model for the comparison of total thyroidectomy (TT) without prophylactic central neck dissection (pCND) (TT alone) and TT with pCND (TT+pCND) strategies applied in patients with clinically nodal negative papillary thyroid carcinoma